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Title of Invention: _____

Inventors (please provide full names): _____

_____

Earliest Priority Filing Date: 6-18-97

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Please search 5-aminolevulinic acid as an agent for diagnosis and treatment of malignant tumors.

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L15            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  "5-AMINOLEVULINIC ACID"/CN
L16              SEL  PLU=ON  L15 1- CHEM :        4 TERMS
L17         5398 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L16
L18         5401 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L17 OR (5(W)AMINOLEVULINIC)(5A
                 )ACID
L19          366 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L18(L)(?TUMOR? OR ?CANCER? OR
                 ?NEOPLAS?)
L20         1512 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L18(L)(?MEDICIN? OR ?DRUG? OR
                 ?THERA? OR ?TREAT? OR ?PHARMA?)
L21          302 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L19 AND L20
L22        27978 SEA FILE=HCAPLUS ABB=ON  PLU=ON  MALIG?(L)(?TUMOR? OR ?CANCER?
                 OR ?NEOPLAS?)
L23           51 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L21 AND L22
L24           31 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L23 NOT (2000 OR 1999 OR 1998
                 OR 1997)/PY


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L24  ANSWER 1 OF 31  HCAPLUS  COPYRIGHT 2001 ACS
ACCESSION NUMBER:         1997:451511  HCAPLUS
DOCUMENT NUMBER:          127:119049
TITLE:                    In-vitro fluorescence kinetics of 5-ALA-induced
                          porphyrin in rat bladder
AUTHOR(S):                Stocker, S.; Heil, P.; Sroka, R.; Baumgartner, R.
CORPORATE SOURCE:         Laser-Forschungslabor, Urologischen Klinik
```

Ludwig-Maximilians-Univ., Munchen, 81377, Germany
SOURCE: Laser Med., Vortr. 10. Tag. Dtsch. Ges. Lasermed. 12. Int. Kongr. (1996), Meeting Date 1995, 113-116. Editor(s): Waidelich, Wilhelm; Staehler, Gerd; Waidelich, Raphaela. Springer: Berlin, Germany. CODEN: 64SGA8
DOCUMENT TYPE: Conference
LANGUAGE: German
AB Knowledge of the time course of protoporphyrin IX (PPIX) synthesis in **malignant** tissue and in normal urothelium after intravesicular instillation of **5-aminolevulinic acid** (5-ALA) is of significance for optimization of photodynamic diagnosis and **therapy** of bladder **tumors**. For detg. **pharmacokinetics**, an in vivo rat model was used employing chem.-induced bladder **neoplasms**. After 5-ALA stimulation, PPIX formed in **tumor** and healthy urothelia within 30 min. In **malignant** tissue, PPIX fluorescence was 1-4-fold higher than in normal urothelium. Max. fluorescence occurred in both tissues at about 3 h. After 30 min, uroporphyrin and coproporphyrin could be detected in bladder fluid.

L24 ANSWER 2 OF 31 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1997:243319 HCAPLUS
DOCUMENT NUMBER: 126:261018
TITLE: Incorporation of 5-ALA (**5-aminolevulinic acid**) in cultivated **cancer** cells and apoptosis cell death by photosensitization of the endogenously-produced Pp-IX
AUTHOR(S): Miyoshi, Norio; Karaya, Kazuhiro; Jin, Zhao-Hui; Ishiguro, Kazumori; Ueda, Keiichi; Fukuda, Masaru
CORPORATE SOURCE: Department of Pathology, Fukui Medical School, Matsuoka, 910-11, Japan
SOURCE: Photomed. Photobiol. (1996), 18, 83-84 CODEN: PHPHEA; ISSN: 0912-232X
PUBLISHER: Japanese Society for Photomedicine and Photobiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The endogenously-produced Pp-IX from the heme precursor 5-amino-levulinic acid (5-ALA) has been used as a new type of photosensitizer. Recently, the photodynamic therapy of non-melanoma **malignant** **tumors** of the skin using the 5-ALA and laser light was studied by Svanberg et al. [Brit. J. Dermat., 130: 743-751 (1994)]. The distribution of the 5-ALA in **cancer** cells is not known. We reported previously that the distribution was mainly in the cytoplasm area in human melanoma cultivated [HMF] cells from the observation of a fluoromicroscope and a fluoromicro spectrophotometer [Photomed.&Photobiol.,17: 135-137 (1995)]. It was found that the 5-ALA would be able to lead to a protoporphyrin-IX (Pp-IX) synthesis from the fluorescence emission spectrum in the cells at the peaks of 638 and 706 nm. We examd. the time course for the incorporation of Pp-IX into the HMF cells changing from 5-ALA to Pp-IX after the 5-ALA addn. to the cells suspended in soln. by means of a fluorescence spectrophotometer. The Pp-IX fluorescence intensity at 638 nm increased until 8 h with incubation time and the intensity level was satd. after 10 h incubation. The fluorescence distribution in the cells was detected mainly at the cytoplasm as a red fluorescence. The cell suspension of a murine and human leukemia (L5178Y and HL-60) cells were irradiated after 8 h incubation with 0.2 mM 5ALA at 630 nm of the wavelength-turnable pulse laser (optical parametric oscillator=OPO laser). The irradiated cells were fixed within 30 min after the irradn. by 70% EtOH, the typical apoptotic phenomena of chromatin condensation and fragmentation were obsd. by an acridine orange (AO) stain. We obsd. a cell population contg. approx. 30% apoptotic cells. These phenomena were confirmed with the TdT-mediated dUTP nick end labeling (TUNEL) technique and the endonucleosomal cleavage 30 min after laser irradn. Furthermore, the rapid DNA cleavage to nucleosome oligomers after PDT within 30 min was obsd., which suggested the initiation of a

late step in the apoptotic process of the leukemia cell. However the apoptotic phenomena in the HMF cell was not obsd.

IT **106-60-5, 5-Aminolevulinic acid**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**5-aminolevulinic acid**-induced protoporphyrin photosensitization of **cancer** cells and apoptosis cell death)

L24 ANSWER 3 OF 31 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1997:73431 HCAPLUS
DOCUMENT NUMBER: 126:154456
TITLE: Topical photodynamic therapy in dermatology
AUTHOR(S): Szeimies, Rolf-Markus; Calzavara-Pinton, PierGiacomo; Karrer, Sigrid; Ortel, Bernhard; Landthaler, Michael
CORPORATE SOURCE: Dep. Dermatology, Univ. Regensburg, Regensburg, D-93402, Germany
SOURCE: J. Photochem. Photobiol., B (1996), 36(2), 213-219
CODEN: JPPBEG; ISSN: 1011-1344
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review, with 43 refs. Although photodynamic **therapy** (PDT) was first used in the **treatment** of skin diseases, phase-III-clin. trials were primarily conducted for the **treatment** of bladder **cancer**, endobronchial and esophageal carcinoma. In dermatol. PDT has most extensively been used for the **treatment** of **malignant** cutaneous lesions. Up to now those patients have been **treated** systemically with first-generation photosensitizers. However, prolonged skin photosensitivity is a major disadvantage of this form of **therapy**. Topical PDT utilizing a variety of sensitizers bypass this unwanted effect. Of strong interest is **5-aminolevulinic acid** (ALA), first introduced in the topical PDT of skin disorders in 1990 by Kennedy and co-workers. ALA serves as a pro-**drug**, i.e., the active photosensitizing compd. is protoporphyrin IX which is synthesized in vivo after exogenous application of ALA. In several oncol. and non-oncol. skin conditions including non-melanoma skin **cancer**, premalignant conditions like actinic keratoses and in psoriasis, topical ALA-PDT showed its effectiveness. Besides ALA, new sensitizers like benzoporphyrines and porphycenes may play a role in topical PDT. However, at the moment, there is still a need for comparative studies and standardized **therapeutic** protocols to define the place of topical PDT in dermatol.

L24 ANSWER 4 OF 31 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1997:73055 HCAPLUS
DOCUMENT NUMBER: 126:154525
TITLE: Inhalation of **5-aminolevulinic acid**: a new technique for fluorescence detection of early stage lung **cancer**
AUTHOR(S): Baumgartner, R.; Huber, R. M.; Schulz, H.; Stepp, H.; Rick, K.; Gamarra, F.; Leberig, A.; Roth, C.
CORPORATE SOURCE: Laser-Forschungslabor Urologischen Klinik, LMU, Munich, 81377, Germany
SOURCE: J. Photochem. Photobiol., B (1996), 36(2), 169-174
CODEN: JPPBEG; ISSN: 1011-1344
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Topical application of **5-aminolevulinic acid** (5-ALA), with subsequent synthesis of protoporphyrin IX (PPIX), is a novel outstanding procedure for photodynamic **treatment**. So far, clin. experience has been reported with creams contg. 5-ALA for the **therapy** of skin **cancer**, oral application for the **treatment** of gastrointestinal disease and intravesical

instillation of 5-ALA solns. for fluorescence detection of superficial bladder **cancer**. Inhalation of 5-ALA for the staining of bronchial **malignancies** is a preferred method in clin. pulmonol. Since no adverse reaction was obsd. in lung function in a canine following inhalation of 5-ALA in increasing concns., clin. applications were performed. Seven patients with pos. or suspicious sputum cytol., but neg. white light bronchoscopy, received 5-10 wt.% 5-ALA in NaCl soln. by means of a medical nebulizer. No side effects were obsd. during and after 5-ALA inhalation. After a period of 3 h, patients underwent fluorescence bronchoscopy using violet light for florescence excitation and an optical multichannel analyzer for fluorescence detection in situ. The results showed fluorescence spectra which could be related to PPIX induced by 5-ALA in the bronchial mucosa. The fluorescence intensity was sufficiently high for video imaging using a target integrating color CCD camera adapted to the flexible bronchoscope. Carcinoma in situ, as well as dysplasias, showed a clear pos. fluorescence. A correlation of fluorescence contrast with histol. on 30 biosies revealed a high sensitivity, but a specifically below 50%. Improvements in light and **drug** dosimetry will form the basis for further clin. trials.

IT **106-60-5, 5-Aminolevulinic acid**
RL: BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**5-aminolevulinic acid** inhalation as new technique for fluorescence detection of early stage lung **cancer**)

L24 ANSWER 5 OF 31 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:663592 HCAPLUS
DOCUMENT NUMBER: 126:4038
TITLE: Evaluation of spectral correction techniques for fluorescence measurements on pigmented lesions in vivo
AUTHOR(S): Sterenborg, H. J. C. M.; Saarnak, A. E.; Frank, R.; Motamedi, M.
CORPORATE SOURCE: Laser Centre, Academic Medical Centre, Amsterdam, Neth.
SOURCE: J. Photochem. Photobiol., B (1996), 35(3), 159-165
CODEN: JPPBEG; ISSN: 1011-1344
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Recently, the use of optical spectroscopy for non-invasive diagnosis of **malignant** melanoma has been suggested. The reliability of such optical measurements can be seriously compromised by spatial variations in the optical properties of the tissue that are not related to **malignancy**. In the present paper we report a novel approach to fluorescence spectroscopy which allows for elimination of spatial variations in the optical properties of the tissue investigated. To test this concept we performed fluorescence and color measurements on moles and unpigmented control skin in human volunteers before and after topical application of .vdelta.-**aminolevulinic acid** (ALA). Two types of fluorescence data anal. were investigated; a single ratio technique based on the ratio of the red to the yellow fluorescence (660-750 nm to 550-600 nm) at 405 nm excitation and a double-ratio technique, the red-to-yellow ratio at 405 nm excitation divided by the red-to-yellow ratio at 435 nm excitation. The two excitation wavelengths were selected to be located close to the max. and at some distance from the Soret excitation band of the porphyrins. The single ratio showed a significant correlation between fluorescence and color. The double ratio was independent of the color of the lesion. These findings indicate that the double-ratio technique is suitable for in-vivo detection of local differences in concn. of fluorescent **tumor**-localizing **drugs** in pigmented lesions. This enables in-vivo studies of the **pharmacokinetics** of **tumor**-localizing agents in pigmented lesions and may significantly contribute to the development of a non-invasive diagnostic tool for **malignant** melanoma.

L24 ANSWER 6 OF 31 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:654588 HCAPLUS
DOCUMENT NUMBER: 126:3876
TITLE: Photodynamic **therapy** using 5-**aminolevulinic acid** for premalignant and malignant lesions of the oral cavity
AUTHOR(S): Fan, Kathleen F. M.; Hopper, Colin; Speight, Paul M.; Buonaccorsi, Giovanni; MacRobert, Alexander J.; Bown, Stephen G.
CORPORATE SOURCE: Medical School, University College London, London, WC1E 6JJ, UK
SOURCE: Cancer (N. Y.) (1996), 78(7), 1374-1383
CODEN: CANCAR; ISSN: 0008-543X
PUBLISHER: Wiley-Liss
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Premalignant changes in the mouth, which are often widespread, are frequently excised or vaporized, whereas **cancers** are **treated** by excision or **radiotherapy**, both of which have cumulative morbidity. Photodynamic **therapy** (PDT) is another option that produces local tissue necrosis with light after prior administration of a photosensitizing agent. This heals with remarkably little scarring and no cumulative toxicity. This article describes the use of PDT with the photosensitizing agent 5-**aminolevulinic acid** (ALA) for premalignant and **malignant** lesions of the mouth. Eighteen patients with histol. proven premalignant and **malignant** lesions of the mouth were sensitized with 60 mg/kg ALA by mouth and **treated** with laser light at 628 nm (100 or 200 J/Cm2). The results were assessed macroscopically and microscopically. Biopsies were taken immediately prior to PDT for fluorescence studies, a few days after PDT to assess the depth of necrosis, when healing was complete, and up to 88 wk later. The depth of necrosis varied from 0.1 to 1.3 mm, but complete epithelial necrosis was present in all cases. All 12 patients with dysplasia showed improvement (repeat biopsy was normal or less dysplastic) and the **treated** areas healed without scarring. Some benefit was obsd. in five of six patients with squamous cell carcinoma, but only two became **tumor** free (one with persistent mild dysplasia). No patient had cutaneous photosensitivity for longer than 2 days. PDT using ALA for dysplasia of the mouth produces consistent epithelial necrosis with excellent healing and is a simple and effective way to manage these patients. In invasive **cancers** are less satisfactory, mainly because the PDT effect is too superficial with current **treatment** regimens using ALA as the photosensitizing agent.
IT **106-60-5, 5-Aminolevulinic acid**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(photodynamic **therapy** using 5-**aminolevulinic acid** for premalignant and malignant lesions of oral cavity in humans)

L24 ANSWER 7 OF 31 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:654029 HCAPLUS
DOCUMENT NUMBER: 125:321795
TITLE: In vitro studies on the potential use of 5-**aminolevulinic acid**-mediated photodynamic **therapy** for gynecological **tumors**
AUTHOR(S): Rossi, F. M.; Campbell, D. L.; Pottier, R. H.; Kennedy, J. C.; Dickson, EF Gudgin
CORPORATE SOURCE: Department Chemistry and Chemical Engineering, Royal Military College Canada, Kingston, ON, K7K 5LO, Can.
SOURCE: Br. J. Cancer (1996), 74(6), 881-887
CODEN: BJCAAI; ISSN: 0007-0920
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Results are reported on the sensitivity of various gynaecol. **tumor** cell lines to **5-aminolevulinic acid**-induced protoporphyrin IX-sensitized photodynamic **therapy** (ALA-PDT) in vitro. All cell lines tested accumulated ALA-induced protoporphyrin IX (PpIX) and demonstrated good sensitivity to ALA-PDT. Localization of PpIX in the mitochondria was demonstrated by fluorescence microscopy. Subcellular damage following ALA-PDT was obsd. using transmission electron microscopy. This damage was localized initially to the mitochondria, with damage to membranes and the nucleus and complete loss of intracytoplasmic organization being obsd. subsequently. There was no apparent difference in ALA-PDT response between a **multidrug**-resistant ovarian carcinoma cell line and its parent line. These results indicate that ALA-PDT has potential for application to **therapy** of gynecol. **malignancies**.

IT **106-60-5, 5-Aminolevulinic acid**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(potential use of **5-aminolevulinic acid** -mediated photodynamic **therapy** for gynecol. **tumors**)

L24 ANSWER 8 OF 31 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:624711 HCAPLUS
DOCUMENT NUMBER: 125:296264
TITLE: Detection of early stages of carcinogenesis in adenomas of murine lung by 5-aminolevulinic acid-induced protoporphyrin IX fluorescence
AUTHOR(S): Campbell, D. L.; Gudgin-Dickson, E. F.; Forket, P. G.; Pottier, R. H.; Kennedy, J. C.
CORPORATE SOURCE: Dep. Pathol., Queen's University, Kingston, ON, Can.
SOURCE: Photochem. Photobiol. (1996), 64(4), 676-682
CODEN: PHCBAP; ISSN: 0031-8655
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Administration of the heme precursor **5-aminolevulinic acid** (ALA) leads to the selective accumulation of the photosensitizer protoporphyrin IX (PpIX) in certain types of normal and abnormal tissues. This phenomenon has been exploited clin. for detection and **treatment** of a variety of **malignant** and nonmalignant lesions. The present preclin. study examd. the specificity of ALA-induced porphyrin fluorescence in chem. induced murine lung **tumors** in vivo. During the early stages of **tumorigenesis** , ALA-induced PpIX fluorescence developed in hyperplastic tissues in the lung and later in early lung **tumor** foci. In early **tumor** foci, max. PpIX fluorescence occurred 2 h after the administration of ALA and returned to background levels after 4 h. There was approx. a 20-fold difference in PpIX fluorescence intensity between **tumor** foci and the adjacent normal tissue. The specificity of ALA-induced fluorescence for hyperplastic tissues and benign **tumors** in lung during **tumorigenesis** suggests a possible use for this fluorochrome in the detection of premalignant alterations in the lung by fluorescence endoscopy. Two non-small cell lung **cancer** cell lines developed ALA-induced PpIX fluorescence in vitro. These lines exhibited a light-dose-dependent phototoxic response to ALA photodynamic **therapy** (PDT) in vitro. Because PpIX is a clin. effective photosensitizer for a wide variety of **malignancies**, these results support the possible use of ALA-induced PpIX PDT for lung **cancer**.

L24 ANSWER 9 OF 31 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:504480 HCAPLUS
DOCUMENT NUMBER: 126:115078
TITLE: Photodynamic therapy: a promising new modality for the treatment of cancer
AUTHOR(S): Schuitmaker, J. J.; Baas, P.; Van Leengoed, H. L. L. M.; Van der Meulen, F. W.; Star, W. M.; Van Zandwijk, N.

CORPORATE SOURCE: Dep. Ophthamol., Univ. Leiden, Leiden, 2333 AL, Neth.
SOURCE: J. Photochem. Photobiol., B (1996), 34(1), 3-12
CODEN: JPPBEG; ISSN: 1011-1344
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB The first reports on photodynamic **therapy** (PDT) due back to the 1970. Since then, several thousands of patients, both with early stage and advanced stage solid **tumors**, have been **treated** with PDT and many claims have been made regarding its efficacy. Nevertheless, the **therapy** has not yet found general acceptance by oncologists. Therefore it seems legitimate to ask whether PDT can still be described as "a promising new **therapy** in the **treatment** of **cancer**". Clin., PDT has been mainly used for bladder **cancer**, lung **cancer** and in **malignant** disease of the skin and upper aerodigestive tract. The sensitizer used in the photodynamic **treatment** of most patients is Photofrin, (Photofrin, the com. name of dihematoporphyrin ether/ester) contg. >80% of the active porphyrin dimers/oligomers (A.M.R. Fisher, A.L. Murphee and C.J. Gomer, clin. and preclin. photodynamic **therapy**, Review Series Article, lasers Surg. Med., 17 (1995) 2-31). It is a complex mixt. of porphyrins derived from hematoporphyrin. Although this sensitizer is effective, it is not most suitable photosensitizer for PDT. Prolonged skin photosensitivity and the relatively low absorbance at 630 nm, a wavelength where tissue penetration of light is not optimal, have been frequently cited as neg. aspects hindering general acceptance. A multitude of new sensitizers is reviewed, with 99 refs., and currently under evaluation. Most of these "second generation photosensitizers" are CP, absorb light at around 650 nm or greater and induce no or less general skin photosensitivity. Another novel approach is the photosensitization of **neoplasms** by the induction of endogenous photosensitizers through the application of **5-aminolevulinic acid** (ALA). This article addresses the use of PDT in the disciplines mentioned above and attempts to indicate developments of PDT which could be necessary for this **therapy** to gain a wider acceptance in the various fields.

L24 ANSWER 10 OF 31 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:459649 HCAPLUS
DOCUMENT NUMBER: 126:115125
TITLE: **Pharmacokinetics** of **5-aminolevulinic-acid**-induced porphyrins in **tumor**-bearing mice
AUTHOR(S): Sroka, R.; Beyer, W.; Gossner, L.; Sassy, T.; Stocker, S.; Baumgartner, R.
CORPORATE SOURCE: Laser-Forschungslabor an der Urologischen Klinik of the University of Munich, Munich, Germany
SOURCE: J. Photochem. Photobiol., B (1996), 34(1), 13-19
CODEN: JPPBEG; ISSN: 1011-1344
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Photodynamic **therapy** and photodynamic diagnosis help to support efficient **treatment** of superficial and early-stage **cancer**. During the last few years, **5-aminolevulinic acid** (5-ALA), a precursor of Hb in the heme biosynthetic pathway, was used to stimulate endogenous porphyrin prodn. In the following the time dependence of 5-ALA-induced porphyrin concn. will be investigated on several tissues in an in-vivo **tumor** model. 5-ALA was administered i.v. at a concn. of 50 mg kg-1 body wt. According to a certain time schedule the animals were sacrificed and 12 different organs as well as the **tumor** were removed. During excitation with the violet light of a Kr+ laser, porphyrin fluorescence spectra in the range 550-750 nm could be detected on the tissue samples. The intensity of the emission spectra at .lambda. = 635.+-.2 nm was taken as a measure of the porphyrin concn. All tissues showed porphyrin

fluorescence. Brightest fluorescence was found on the **tumor**. A max. contrast of the fluorescence intensity between the **tumor** and the non-**malignant** organs of up to 30 was obsd. at 4-6 h post-injection. The kinetics of the porphyrin concn. depend on the organ. Simple math. models will be derived and discussed.

IT **106-60-5, 5-Aminolevulinic acid**
RL: BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**pharmacokinetics** of **5-aminolevulinic-acid**-induced porphyrins in **tumor**-bearing mice)

L24 ANSWER 11 OF 31 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:434569 HCAPLUS
DOCUMENT NUMBER: 125:136573
TITLE: Usefulness of fluorescence photodetection of **neoplastic** urothelial foci in bladder **cancer** following intravesical instillation of **delta-aminolevulinic acid** (5-ALA).
AUTHOR(S): Jichlinski, Patrice; Forrer, Martin; Mizeret, Jerome; Braichotte, Daniel; Wagnieres, Georges; Zimmer, Georges; Guillou, Louis; Schmidlin, Franz; Graber, Peter; et al.
CORPORATE SOURCE: Department of Urology, CHUV Hospital, Lausanne, CH-1011, Switz.
SOURCE: Proc. SPIE-Int. Soc. Opt. Eng. (1996), 2671(Lasers in Surgery: Advanced Characterization, Therapeutics, and Systems VI), 340-347
CODEN: PSISDG; ISSN: 0277-786X
DOCUMENT TYPE: Journal
LANGUAGE: English

AB An excellent knowledge of histopathol. risk factors of superficial bladder transitional cell carcinoma is mandatory to establish the prognosis of the disease. Presence or absence of carcinoma in situ (CIS) in superficial bladder **cancer** is one of the most powerful risk indicator. This study examines the usefulness of fluorescence photodetection of **neoplastic** urothelial foci in bladder **cancer** following intravesical instillation of **.delta.-aminolevulinic acid** (5-ALA). Following bladder instillation of an aq. soln. of 5-ALA in 43 cases, a Krypton ion laser and a Xenon arc-lamp were successively used as excitation source of the PPIX fluorescence. Tissue samples were resp. taken during bladder wall photodetection, either by means of a video camera or under direct endoscopic observation. A good correlation was obsd. between the fluorescence findings and the histopathol. diagnosis. On a total of 298 biopsies, 49/110 carcinomatous lesions were detected by the fluorescence and more than 36% were CIS. PPIX induced fluorescence with topical bladder instillation of 5-ALA is an efficient and useful method of mapping the mucosa in bladder carcinoma. Moreover, in case of a multifocal disease, this method seems very helpful in finding and **treating** any residual **malignant** spots at the end of a transurethral bladder resection.

IT **106-60-5, .delta.-Aminolevulinic acid**
RL: BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(fluorescence photodetection of bladder **cancer** with **.delta.-aminolevulinic acid** intravesical instillation)

L24 ANSWER 12 OF 31 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:418678 HCAPLUS
DOCUMENT NUMBER: 125:109037
TITLE: Interstitial photodynamic **therapy** of canine prostate with meso-tetra-(m-hydroxyphenyl) chlorin and **5-aminolevulinic acid**: A preliminary study
AUTHOR(S): Chang, Shi-Chung; Buonaccorsi, Gio; MacRobert,

Alexander J.; Bown, Stephen G.
CORPORATE SOURCE: Medical School, University College London, London, UK
SOURCE: Proc. SPIE-Int. Soc. Opt. Eng. (1996), 2625(Photochemistry: Photodynamic Therapy and Other Modalities), 224-231
CODEN: PSISDG; ISSN: 0277-786X
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Photodynamic **therapy** (PDT) is proved to have potential for managing various **malignancies**. We investigated tissue biodistribution and photodynamic effects on a canine model in vivo using second generation photosensitizers, meso-tetra(m-hydroxyphenyl)chlorin (mTHPC) and **5-aminolevulinic acid** (ALA) to evaluate the feasibility and possible future application of PDT on the prostate. Using fluorescence microscopy, the optimal sensitization time of the prostate was between 24-72 h with mTHPC and, 3 h with ALA. After optimum time of sensitization, prostates of mature beagle were **treated** with laser at various sites by placing fiber interstitially under the guidance of transrectal ultrasound. The light dose for each **treatment** site was 100 J (100 mW for 1000 s at the wavelength of 650 and 630 nm, resp.). With mTHPC, single laser fiber was able to induce organ confined PDT lesion as large as 20.times.18.times.18 mm in size. However, the PDT lesion with ALA was negligible 3 days after **treatment**. Phys. distress manifested as urinary retention, poor appetite and body wt. loss, was more prominent with increasing no. of **treatment** sites as a result of extensive prostatic swelling and urethral damages. However, these problems usually alleviated spontaneously 7 to 10 days after PDT. The characteristic histol. changes were hemorrhagic necrosis and glandular destruction with preservation of interlobular collagen fibers. Urethral damage seen at the early stage healed by regeneration of urothelium in 4 wk. We conclude that interstitial PDT with mTHPC is tech. possible to produces extensive glandular necrosis in the normal prostate which heals safely and does not change the prostatic architecture. ALA, although seems promising for bladder **tumors**, is much less effective than mTHPC on the prostate. With mTHPC, it might have the potential for **treating** prostate **cancers** localized in the periphery of the gland.

IT **106-60-5, 5-Aminolevulinic acid**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(interstitial photodynamic **therapy** of canine prostate with meso-tetra-(m-hydroxyphenyl)chlorin and **5-aminolevulinic acid**)

L24 ANSWER 13 OF 31 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:418674 HCAPLUS
DOCUMENT NUMBER: 125:109033
TITLE: Photodegradation of sensitizers in mouse skin during PCT
AUTHOR(S): Moan, J.; Iani, V.; Ma, L. W.; Peng, Q.
CORPORATE SOURCE: Department Biophysics, Institute Cancer Research, Oslo, 0310, Norway
SOURCE: Proc. SPIE-Int. Soc. Opt. Eng. (1996), 2625(Photochemistry: Photodynamic Therapy and Other Modalities), 187-193
CODEN: PSISDG; ISSN: 0277-786X
DOCUMENT TYPE: Journal
LANGUAGE: English

AB All photosensitizers applied in exptl. and clin. **photochemotherapy** (PCT) of **cancer** are degraded during light exposure. Under certain conditions this may be a disadvantage since larger light fluences are needed to destroy the **malignant** tissue. However, photodegrdn. may also offer an advantage:. If the applied dose of sensitizer is so low that most of it is photodegraded before normal tissue is destroyed, but still large enough to sensitize the **tumor** to destruction, one may achieve a larger **tumor** to normal tissue

therapeutic ratio than when using a higher dose of sensitizer. **Tumors** usually contain two to ten times higher concns. of sensitizers than do the surrounding normal tissues. We have studied the photodegrdn. of a no. of sensitizers, including Photofrin (PII), benzoporphyrin deriv. mono acid ring A (BPD), chlorin e6 (Chle6), **5-aminolevulinic acid** (ALA)-induced protoporphyrin IX (PpIX), meso-tetrahydroxyphenylchlorin (m-THPC), meso-tetrahydroxyphenylporphyrin (m-THPP) tetraphenylporphine tetrasulfonated (TPPS4), aluminum phthalocyanine disulfonated (AlPcS2), tetrasulfonated (AlPcS4) and zinc phthalocyanine (ZnPc) in liposomes. The sensitizers were injected in Balb/c nude mice and exposed to light from an argon pumped dye laser, tuned to the appropriate **therapeutic** wavelength at a fluence rate of 100 mW/cm2. The sensitizer fluorescence in the laser-exposed skin was monitored by a fiber-optic probe coupled to a fluorescence spectrometer. The kinetics of the fluorescence decay during PCT were, in all cases, nonexponential but differed from dye to dye. Chle6 and m-THPC were found to be the most photolabile sensitizers. AlPcS4 and AlPcS2 and, to a minor degree, TPPS4 showed a peculiar fluorescence increase during PCT, similar to what we have found earlier for these sensitizers in cells in vitro. The fluorescence increase is indicative of lysosomal localization and perforation of the lysosomes during PCT.

L24 ANSWER 14 OF 31 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:418655 HCAPLUS
DOCUMENT NUMBER: 125:109016
TITLE: Photodynamic **therapy** with 5-**aminolevulinic acid**: Basic principles and applications
AUTHOR(S): Pottier, Roy; Kennedy, James C.
CORPORATE SOURCE: Department Chemistry and Chemical Engineering, Royal Military College Canada, Kingston, ON, K7K 5L0, Can.
SOURCE: Proc. SPIE-Int. Soc. Opt. Eng. (1996), 2625(Photochemistry: Photodynamic Therapy and Other Modalities), 2-10
CODEN: PSISDG; ISSN: 0277-786X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Numerous photosensitizing pigments that absorb visible light and are selectively retained in **neoplastic** tissue are being investigated as potential **photochemotherapeutic** agents. While much emphasis is being placed on the synthesis of new, far-red absorbing photosensitizers, an alternative approach has been to stimulate the human body to produce its own natural photosensitizer, namely protoporphyrin IX (PpIX). Exogenous **5-aminolevulinic acid** (ALA) will be rapidly bioconverted into PP by mitochondria, the process being particularly efficient in **tumor** cells. Since PpIX has a natural and rapid clearing mechanism (via. the capture of iron in the process of being converted into heme), ALA-PDT does not suffer from lingering skin phototoxicity. ALA may be introduced orally, i.v. or topically, and ALA-PDT has been shown to be effective in the **treatment** of both **malignant** and non-**malignant** lesions.
IT **106-60-5, 5-Aminolevulinic acid**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**tumor** photodynamic **therapy** with 5-**aminolevulinic acid**-induced protoporphyrin IX: basic principles and applications)

L24 ANSWER 15 OF 31 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:279933 HCAPLUS
DOCUMENT NUMBER: 125:29213
TITLE: Does .delta.-aminolevulinic acid induce genotoxic effects?
AUTHOR(S): Fiedler, Dagmar M.; Eckl, Peter M.; Krammer, Barbara

CORPORATE SOURCE: University of Salzburg, Institute of Physics and Biophysics, Hellbrunnerstr. 34, Salzburg, A-5020, Austria
SOURCE: J. Photochem. Photobiol., B (1996), 33(1), 39-44
CODEN: JPPBEG; ISSN: 1011-1344
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **5-Aminolevulinic acid** (ALA) is a precursor of protoporphyrin IX (PpIX) in the biosynthetic pathway for heme. The presence of exogenous ALA bypasses the feedback control and may induce the accumulation of PpIX. Since heme-contg. enzymes are essential for energy metab., every nucleated cell in the body must have at least a minimal capacity to synthesize PpIX. Photodynamic **therapy** (PDT), which is the **treatment** of **malignant** lesions with light following the administration of a **tumor**-localizing photosensitizer, leads to oxidative damage, including the formation of genotoxic membrane degrdn. products via lipid peroxidn. In addn., it has been demonstrated that ALA itself can form the reactive oxygen species O2.bul.-, H2O2 and OH.bul. by autoxidn., suggesting that it could potentially induce DNA damage. Therefore cultures of rat hepatocytes, which have been demonstrated to be very sensitive indicators for genotoxic effects induced by the lipid peroxidn. product 4-hydroxynonenal and analogous aldehydes, were examd. for possible mutagenic effects after **treatment** with ALA in the absence of light. The cytogenetic endpoints detd. were chromosomal aberrations and the induction of micronuclei. Compared with the controls, significantly elevated levels of chromosomal aberrations and micronuclei were obsd. at concns. of 1 .mu.g ml-1 or greater. Chromosomal aberrations and micronuclei were found to increase up to a concn. of 100 .mu.g ml-1 ALA. While micronuclei decrease at higher concns., chromosomal aberrations remain at the same level. The kinetics of PpIX formation after induction with 100 and 1000 .mu.g ml-1 ALA appear to be the same for both concns., suggesting that the induction of chromosomal aberrations may be due to PpIX.

L24 ANSWER 16 OF 31 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:160505 HCAPLUS
DOCUMENT NUMBER: 124:225249
TITLE: Intracellular distribution of a heme precursor (ALA) in a human melanoma cultivated cell (HME) and process of the photocytotoxic damage
AUTHOR(S): Miyoshi, Norio; Ishiguro, Kazumori; Ueda, Keiichi; Fukuda, Masaru
CORPORATE SOURCE: Department Pathology, Fukui Medical School, Japan
SOURCE: Photomed. Photobiol. (1995), 17, 135-7
CODEN: PHPHEA; ISSN: 0912-232X
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Recently, photodynamic **therapy** of non-melanoma **malignant tumors** of the skin using a topical heme precursor **5-aminolevulinic acid** (ALA) sensitization and laser light had be done by Svanberg et al. [Brit. J. Dermat., 130: 743-751 (1994)]. It is unclear for the distribution of the ALA in a **cancer** cell. We examd. the observation for the distribution of a heme precursor ALA in a human melanoma cultivated cell (HMF) by a fluoromicroscope or a fluoromicrospectroscope, and the photocytotoxicity of HMF damaged by the photosensitization of ALA was obsd. using a pace-contrast microscope. In the result, it was found that the ALA would be able to change to protoporphyrin IX (Pp-IX) even in the cultivated cell from the fluorescence emission spectra at the peaks of 636 and 706 nm. It was considered that ALA mols. were metabolized at even if a cultivated cell to emit the protoporphyrin IX (Pp-IX) fluorescence. It will be mainly at the cytoplasm area from the observation by a fluoromicroscope. The cytoplasm area was the largest damage in the cell. It was considered that the nuclear membrane was also damaged by the photosensitization from the distribution phenomena of calcium in the cytoplasm area changed to the nuclear region.

L24 ANSWER 17 OF 31 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:68150 HCAPLUS
DOCUMENT NUMBER: 124:169723
TITLE: Fluorescence cystoscopy following intravesical instillation of **5-aminolevulinic acid**: A new procedure with high sensitivity for detection of hardly visible urothelial **neoplasias**
AUTHOR(S): Kriegmair, M.; Stepp, H.; Steinbach, P.; Lumper, W.; Ehsan, A.; Stepp, H. G.; Rick, K.; Knuechel, R.; Baumgartner, R.; Hofstetter, A.
CORPORATE SOURCE: Urologische Klinik, Ludwig-Maximilians-Universitat, Munich, D-81377, Germany
SOURCE: Urol. Int. (1995), 55(4), 190-6
CODEN: URINAC; ISSN: 0042-1138
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Methods have been sought for the in vivo marking of tiny papillary **tumors** of the bladder and flat urothelial lesions such as dysplasia or carcinoma in situ, which can easily be missed during conventional endoscopy under white light. A new procedure is reported for the fluorescence detection of urothelial dysplasia and early bladder **cancer**. The method is based on intravesical application of **5-aminolevulinic acid** (ALA). ALA if applied exogenously induces accumulation of protoporphyrin IX (PPIX) in the urothelium of the bladder. PPIX is an intensively red fluorescing agent. The mean ratio of fluorescence intensity between urothelial **cancer** and normal epithelium was found to be 17:1. Fluorescence excitation was achieved by violet light from a krypton ion laser (.lambda. = 406.7 nm) or from a xenon arc lamp with a bandpass filter system (.lambda. = 375-440 nm). Both light sources proved to be of equal suitability for fluorescence excitation. Fluorescence microscopy revealed that the PPIX fluorescence is strictly limited to the urothelium. It could not be detected from the submucosa or muscle of the bladder. Bladder wall biopsies were taken from 90 patients with suspicion of bladder **cancer** under fluorescence view. The fluorescence detection proved to be of high sensitivity (98%). No serious side effects which would preclude further clin. testing, esp. no cutaneous photoreaction, were obsd. **Tumor**-assocd. fluorescence induced by topical ALA application offers new perspectives in the diagnosis and **treatment** of bladder **cancer**. In case of suspicious or pos. urine cytol. findings, ALA fluorescence cystoscopy may be useful for detecting the precise site of the **malignancy**. The procedure might be helpful in complete resection or coagulation of urothelial **neoplasms**. Due to this, diminishing recurrence rates are expected. However, this hypothesis has to be studied in prospective clin. trials.
IT **106-60-5, 5-Aminolevulinic acid**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(fluorescence cystoscopy following intravesical instillation of **5-aminolevulinic acid** and detection of hardly visible urothelial **neoplasias**)

L24 ANSWER 18 OF 31 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1995:962697 HCAPLUS
DOCUMENT NUMBER: 124:80916
TITLE: Cellular fluorescence of the endogenous photosensitizer protoporphyrin IX following exposure to 5-aminolevulinic acid
AUTHOR(S): Steinbach, Pia; Weingandt, Helmut; Baumgartner, Reinhold; Kriegmair, Martin; Hofstaedter, Ferdinand; Knuechel, Ruth
CORPORATE SOURCE: Department Pathology, University Regensburg, Regensburg, D-93042, Germany
SOURCE: Photochem. Photobiol. (1995), 62(5), 887-95
CODEN: PHCBAP; ISSN: 0031-8655

DOCUMENT TYPE: Journal
LANGUAGE: English
AB Supplying **5-aminolevulinic acid** (ALA), a precursor in the biosynthetic pathway to heme, from an external source leads to an accumulation of the endogenous fluorescent photosensitizer protoporphyrin IX (PPIX). Following instillation of ALA in the urinary bladder, **neoplastic** tissue can be discerned by fluorescence cystoscopy or **treated** by illumination with light of an appropriate wavelength. To provide a biol. rationale for the clin. findings, the authors have analyzed the capacity of three different cell lines to accumulate PPIX by flow cytometry. Three different urothelial cell lines, normal fibroblasts and endothelial cells were exposed to ALA under varying conditions. Urothelial cell lines J82 and RT4, derived from **malignancies** of the bladder displayed fluorescence intensities 9- and 16-fold, resp., above the fluorescence level of the normal urothelial cell line HCV29. Human umbilical cord endothelial cells fluoresced moderately while the fibroblast cell line N1 exhibited a fluorescence level comparable to those of the **cancer** cells. Fluorescence increased with increasing cell d. and was also dependent on the growth of cells as monolayers or multicellular spheroids. Increasing ALA concns. led to satn. of fluorescence after 4 h of incubation at cell type-specific fluorescence levels obtained at different ALA concns. Continuous incubation in medium contg. serum resulted in a linear rise of fluorescence during the first 4 h, which was followed by a satn. period (8-24 h) and a renewed rise. In the case of serum depletion, fluorescence intensities were significantly higher and increased linearly during the entire 48 h incubation period. By replacing serum with albumin, it could be shown that the emission of PPIX into the medium in the presence of serum is mainly caused by this protein. The ALA-induced fluorescence was predominantly perinuclear after 4 h of incubation and relocated toward the cell membrane after prolonged incubation. This study demonstrated the complexity of factors influencing the ALA-induced fluorescence and should stimulate further research in this field.

L24 ANSWER 19 OF 31 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1995:741983 HCAPLUS
DOCUMENT NUMBER: 123:192532
TITLE: The effect of photodynamic therapy on the mechanical integrity of normal rabbit carotid arteries
AUTHOR(S): Grant, W. E.; Buonaccorsi, G.; Speight, P. M.; MacRobert, A. J.; Hopper, C.; Bown, S. G.
CORPORATE SOURCE: Department of Surgery, University College London Medical School, London, UK
SOURCE: Laryngoscope (1995), 105(8, Pt. 1), 867-71
CODEN: LARYA8; ISSN: 0023-852X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Photodynamic **therapy** (PDT) for **tumor** ablation is effective in the **treatment** of superficial **cancers**. Adjunctive intraoperative PDT has been proposed for the "sterilization" of **tumor** beds after the resection of **malignancies**. Arteries in photosensitized animal models exposed to appropriate light receive characteristic injury. This study was conducted to det. whether photodynamic injury to the rabbit carotid artery results in thrombotic occlusion or weakening of the vessel wall. PDT of the carotid arteries of New Zealand white rabbits, using either disulfonated aluminum phthalocyanine or **5-aminolevulinic-acid** -induced protoporphyrin IX as the photosensitizer, was performed with a light dose of 100 J/cm2. Histol. examn. of the carotids **treated** with either agent demonstrated typical full-thickness loss of cellularity 3 days after PDT. All vessels remained patent, and no inflammatory infiltrate was evident. Elastin van Gieson staining showed preservation of inner and medial elastic laminae and medial and adventitial collagen. Addnl. rabbits were similarly **treated** with PDT to 1-cm segments of both common carotid arteries. The animals were sacrificed at 3, 7, and 21 days. The carotids were exposed, and both control and **treated**

segments were subjected to intraluminal hydrostatic distention until the vessels burst. No redn. in the pressure required to burst the vessels was evident in the **treated** vessels as compared with the control vessels. The authors of the study concluded that despite full-thickness cell death, PDT-**treated** arteries are not at risk for thrombotic occlusion or hemorrhage.

IT **106-60-5, 5-Aminolevulinic acid**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(photodynamic **therapy** effect on carotid artery mech. integrity)

L24 ANSWER 20 OF 31 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1995:626735 HCAPLUS
DOCUMENT NUMBER: 123:106678
TITLE: **Pharmacokinetic** studies of **.delta .-aminolevulinic acid**-induced protoporphyrin IX build-up in some **malignant tumors**
AUTHOR(S): Svanberg, Katarina; Clemente, Laudelina Pais; Clemente, Manuel Pais; Wang, Ingrid; Warloe, Trond; Andersson-Engels, Stefan; Berg, Roger; Moan, Johan; Peng, Qian; Svanberg, Sune
CORPORATE SOURCE: Dept. of Oncology, Lund University Hospital, Lund, S-221 85, Swed.
SOURCE: Proc. SPIE-Int. Soc. Opt. Eng. (1995), 2387, 30-42
CODEN: PSISDG; ISSN: 0277-786X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Laser-induced fluorescence was used for the monitoring of **.delta .-aminolevulinic acid** (ALA)-induced protoporphyrin IX (PpIX) build-up in non-melanoma **malignant tumors** of the skin and some **cancers** in the head and neck region. An optical-fiber based point monitoring system was utilized in the recording of fluorescence spectra at different time intervals after the administration of ALA. In the cases of skin **tumors** ALA was normally applied topically to the area. Only in one patient with an aggressive skin **tumor** ALA was administered i.v. For the PpIX induction in head and neck **tumors** ALA was given orally. An example of a **tumor** fluorescence image is also presented.

IT **106-60-5, .delta.-Aminolevulinic acid**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**.delta.-aminolevulinic acid**-induced protoporphyrin IX build-up in some **malignant tumors**

L24 ANSWER 21 OF 31 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1995:583708 HCAPLUS
DOCUMENT NUMBER: 123:78606
TITLE: Exogenous .delta.-aminolevulinic acid induces porphyrin biosynthesis in human skin organ cultures with different porphyrin patterns in normal and malignant human tissue
AUTHOR(S): Fritsch, Clemens; Batz, Janine; Bolsen, Klaus; Schulte, Klaus; Ruzicka, Thomas; Goerz, Guenter
CORPORATE SOURCE: Department Dermatology, Heinrich Heine University, Duesseldorf, 40 225, Germany
SOURCE: Proc. SPIE-Int. Soc. Opt. Eng. (1995), 2371, 215-20
CODEN: PSISDG; ISSN: 0277-786X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The carboxylation state of porphyrin metabolites causes their hydrophilic or lipophilic properties and subsequently their distribution in tissues, cells and subcellular compartments. The profile of porphyrin metabolites

neither in normal skin nor in **malignant** skin **tumors** after administration of .**delta.-aminolevulinic acid** has been studied in detail, yet. Explant cultures of normal skin and **neoplastic** tissues, e.g. keratoakanthoma and basal cell carcinoma, were incubated with 1 mM ALA for 36 h. Total porphyrin concn. and percentage of porphyrin metabolites were detd. quant. in tissues and corresponding supernatants. 70-90% of total porphyrins could be detected in the supernatants of all samples. The highly carboxylated porphyrins were the prevailing metabolites in the supernatants as well as in the tissues. The basal cell carcinoma produced significantly more protoporphyrin and the keratoakanthoma significantly more coproporphyrin as compared to normal skin. The results show that explant cultures offer an easy approach to examine the enzymic capacity in porphyrin biosynthesis of various tissues. Benign and **malignant** human tissues produce different porphyrin metabolites, which may be useful for selective and more effective photodynamic diagnosis or **therapy**.

L24 ANSWER 22 OF 31 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1995:579899 HCAPLUS
DOCUMENT NUMBER: 123:4739
TITLE: The role of transferrin receptor (CD71) in photodynamic **therapy** of activated and malignant lymphocytes using the heme precursor .**delta.-aminolevulinic acid** (ALA)
AUTHOR(S): Rittenhouse-Diakun, K.; van Leengoed, H.; Morgan, J.; Hryhorenko, E.; Paszkiewicz, G.; Whitaker, J. E.; Oseroff, A. R.
CORPORATE SOURCE: Dep. Dermatology, Roswell Park Cancer Inst., Buffalo, NY, 14263, USA
SOURCE: Photochem. Photobiol. (1995), 61(5), 523-8
CODEN: PHCBAP; ISSN: 0031-8655
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Endogenously generated protoporphyrin IX (PpIX) from exogenous ALA can be an effective photosensitizer. PpIX accumulation is inversely dependent on available intracellular iron, which is required for the conversion of PpIX to heme. Iron also is necessary for cell replication. Since iron can be toxic, intracellular iron levels are tightly controlled. Activated and proliferating cells respond to the demand for intracellular iron by upregulating membrane expression of the transferrin receptor (CD71) which is needed for iron uptake. We predicted that activated lymphocytes (CD71+) would preferentially accumulate PpIX because of their lower intracellular iron levels and because of competition for iron between ALA-induced heme prodn. and cellular growth processes. Thus, the CD71+ cells could serve as PDT targets. Stimulation of human peripheral blood lymphocytes (PBL) with the mitogens, phytohemagglutinin A, Con A and pokeweed prior to incubation with ALA results in PpIX accumulation correlating with level of activation. Activated lymphocytes expressing high levels of our face CD71 transferrin receptors generated more PpIX than those with low CD71 expression. Incubating activated cells in transferrin depleted medium (thereby decreasing the iron availability) further increased PpIX levels. Malignant, CD71 + T lymphocytes from a patient with cutaneous T-cell lymphoma (CTCL)/Sezary syndrome also accumulated increased PpIX levels in comparison to normal lymphocytes. PDT of activated lymphocytes and Sezary cells after ALA incubation demonstrated preferential killing compared to normal, unstimulated PBL. These findings suggest a possible mechanism for the selectivity of ALA PDT for activated CD71 + cells. They also indicate a clin. use for ALA-PDT in therapy directed towards the malignant lymphocytes in leukemias and lymphomas, and as an immunomodulatory agent.

IT **106-60-5, .delta.-Aminolevulinic acid**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(transferrin receptor (CD71) role in photodynamic **therapy** of activated and malignant lymphocytes using heme precursor .**delta.-aminolevulinic acid** (ALA))

L24 ANSWER 23 OF 31 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1994:625157 HCAPLUS
DOCUMENT NUMBER: 121:225157
TITLE: A mechanistic study of cellular photodestruction with 5-aminolevulinic acid-induced porphyrin
AUTHOR(S): Iinuma, S.; Farshi, S.S.; Ortel, B.; Hasan, T.
CORPORATE SOURCE: Wellman Laboratories of Photomedicine and Department of Dermatology, Harvard Medical School, Boston, MA, 02114, USA
SOURCE: Br. J. Cancer (1994), 70(1), 21-8
CODEN: BJCAAI; ISSN: 0007-0920
DOCUMENT TYPE: Journal
LANGUAGE: English
AB 5-Aminolaevulinic acid (ALA)-induced porphyrin biosynthesis and phototoxicity in vitro was investigated in five **malignant** and two normal cell lines. Intracellular protoporphyrin IX (PpIX) content was quantified by extn. and fluorescence spectroscopy. Cellular PpIX content did not always correlate with cell proliferation rate as measured by the doubling times of cell lines. Cellular efflux of PpIX was also investigated. In a bladder carcinoma cell line, the obsd. rapid efflux was not blocked by verapamil, an inhibitor of the P-glycoprotein efflux pump. These data support the view that cellular PpIX accumulation is a dynamic process that is detd. by both the efflux of PpIX from the cells and enzyme activities in the heme biosynthesis pathway. Desferrioxamine (desferal), a modulator of PpIX biosynthesis, enhanced ALA-induced cellular PpIX content significantly in all carcinoma cell lines but not in nonmalignant cell lines. The enhanced PpIX cellular accumulation is attributed to inhibition of ferrochelatase activity, the enzyme responsible for the conversion of PpIX to heme. PpIX-mediated cellular photodestruction following irradn. with an argon ion laser at 514.5 nm was detd. by the 'MTT assay'. There appeared to be a 'threshold' effect of cellular PpIX content; cells that synthesized less than 140 ng .mu.g-1 protein exhibited very little phototoxic damage, while cell lines having greater than 140 ng PpIX .mu.g-1 protein exhibited a consistent phototoxic response. Among the cell lines which did undergo phototoxic damage, there was not a strict correlation between PpIX cellular content and ALA-induced phototoxicity. Desferal enhanced the PpIX content and phototoxic effect in the responsive cells. Fluorescence microscopy of the ALA-treated cells revealed marked accumulation of PpIX in mitochondria (rhodamine 123 costaining). That the primary site of phototoxic damage is also the mitochondria was confirmed by electron micrographs of cells photosensitized with ALA-induced PpIX, which showed swelling of mitochondria within minutes after irradn. while other suborganelles appeared to be unaffected. The repair or further destruction of the mitochondria was fluence and cell-type dependent. The data from this study suggest that the basis of increased ALA-induced PpIX accumulation in **tumors** is a combination of various aspects of the metabolic process and pharmacokinetics and that the efficacy of photodestruction of **malignancy** will be detd. not only by the rate of PpIX synthesis but also by specific cellular and tissue characteristics.

L24 ANSWER 24 OF 31 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1994:574080 HCAPLUS
DOCUMENT NUMBER: 121:174080
TITLE: Using **.delta.-aminolevulinic acid** in **cancer therapy**
AUTHOR(S): Kennedy, James C.; Pottier, Roy H.
CORPORATE SOURCE: Dep. Oncol., Queen's Univ., Kingston, ON, K7L 3N6, Can.
SOURCE: ACS Symp. Ser. (1994), 559(Porphyric Pesticides), 291-302
CODEN: ACSMC8; ISSN: 0097-6156
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The administration of an appropriate dose of 5-

aminolevulinic acid (ALA) to patients with certain types of **cancer** leads to the preferential accumulation of fluorescing and/or photosensitizing concns. of protoporphyrin IX (Proto IX) within the **malignant** cells. Subsequent exposure of such **cancers** to photoactivating light may cause selective destruction of the **malignant** tissue by photodynamic action, with sparing of adjacent normal tissues.

IT **106-60-5, .delta.-Aminolevulinic acid**
RL: BIOL (Biological study)
(photodynamic **therapy** with, of **cancer**)

L24 ANSWER 25 OF 31 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1993:466733 HCAPLUS
DOCUMENT NUMBER: 119:66733
TITLE: Comparison of aluminum sulfonated phthalocyanine with 5-aminolevulinic acid induced protoporphyrin IX: tissue distributions, photodamage and photodegradation
AUTHOR(S): MacRobert, A. J.; Bedwell, J.; Loh, C. S.; Chatlani, P. T.; Bown, S. G.
CORPORATE SOURCE: Med. Sci., Univ. Coll. London, London, UK
SOURCE: Proc. SPIE-Int. Soc. Opt. Eng. (1993), 1881(Proceedings of Optical Methods for Tumor Treatment and Detection: Mechanisms and Techniques in Photodynamic Therapy II, 1993), 296-304
CODEN: PSISDG; ISSN: 0277-786X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Flurorescence spectroscopic studies have been carried out on tissue sensitization by aluminum sulfonated phthalocyanine (AlSPc) and endogenous protoporphyrin IX induced by administration of exogenous **5-aminolevulinic acid** (ALA). A charge-coupled device (CCD) imaging system has been used to obtain quant. fluorescence distributions of sensitization in frozen sections taken from rat **tumors** together with normal adjacent tissues. Using ALA, specific porphyrin sensitization of **malignant** epithelium is obsd. with much less sensitization present in connective tissue. Photodegrdn. of AlSPc and PPIX was studied by monitoring of fluorescence bleaching: in normal rat colon, there is a significant redn. in AlSPc fluorescence at the edge of the photonecrosed zone which suggests that photodegrdn. may provide a means of diagnosing the extent of tissue damage. ALA-induced PPIX fluorescence is also obsd. to bleach in colon simultaneously with an increase in fluorescence emission near 675 nm which is attributed to a photoprotoporphyrin degrdn. product.

IT **106-60-5, 5-Aminolevulinic acid**
RL: BIOL (Biological study)
(photodynamic **therapy** with, of colon **tumor**, protoporphyrin induction in, aluminum sulfonated phthalocyanine comparison with)

L24 ANSWER 26 OF 31 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1993:66752 HCAPLUS
DOCUMENT NUMBER: 118:66752
TITLE: Potential of liposome-entrapped **aminolevulinic acid** in **cancer therapy**. Effect of prior injection of empty liposomes and different routes of administration
AUTHOR(S): Fukuda, H.; Paredes, S.; Casas, A.; Chueke, F.; Batlle, A. M. del C.
CORPORATE SOURCE: Cent. Invest. Porfirinas Porfirias, UBA, Buenos Aires, 1428, Argent.
SOURCE: Cancer J. (1992), 5(5), 295-9
CODEN: CANJEI; ISSN: 0765-7846
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The potential use of a liposome-encapsulated porphyrin precursor, **delta aminolevulinic acid** (ALA), for diagnosis

and **treatment** of **malignancy** was evaluated. With this aim, in-vivo porphyrin synthesis by **tumor** and other tissues from mammary adenocarcinoma-bearing mice, receiving liposome-encapsulated ALA by i.p. and **intratumoral** (i.t.) routes with or without previous injection of unloaded phospholipid vesicles, at different times over 24 h after injection, was examd. It was found that administration of empty liposomes enhanced the level of porphyrins accumulated in **tumor** when ALA (240 mg/kg) was injected either i.p. or i.t.. Rapid clearance of porphyrins occurred, so 24 h after injection of ALA, basal levels were found in almost all tissues examd. These results, together with the fact that a **tumor**-to-skin porphyrin concn. ratio as nigh as 28 was obtained, support our proposal for the potential use of liposome-entrapped ALA for early diagnosis and photodynamic **therapy** of **malignant** cells.

IT **106-60-5, .DELTA.-Aminolevulinic acid**
RL: BIOL (Biological study)
(liposome-encapsulated, **antitumor** activity of, against mammary gland adenocarcinoma)

L24 ANSWER 27 OF 31 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1993:3124 HCAPLUS
DOCUMENT NUMBER: 118:3124
TITLE: Photodynamic **therapy** of the normal rat stomach: a comparative study between di-sulfonated aluminum phthalocyanine and 5-**aminolevulinic acid**
AUTHOR(S): Loh, C. S.; Bedwell, J.; MacRobert, A. J.; Krasner, N.; Phillips, D.; Bown, S. G.
CORPORATE SOURCE: Gastroenterol. Unit., Walton Hosp., Liverpool, L9 1AE, UK
SOURCE: Br. J. Cancer (1992), 66(3), 452-62
CODEN: BJCAAI; ISSN: 0007-0920
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Dysplasia in the upper gastrointestinal tract carries a risk of invasive **malignant** change. Surgical excision of the affected organ is the only **treatment** available. Photodynamic **therapy** has been shown to be promising in the **treatment** of early and superficial **tumors** and may be useful for the ablation of dysplastic mucosa. Because of the diffuse nature of the disease, such **treatment** would necessarily involve destruction of large areas of mucosa and it is desirable to confine its effect to the mucosa in order that safe healing can take place. By means of photometric fluorescence microscopy, the pattern of photosensitization was studied in the normal rat stomach using disulfonated aluminum phthalocyanine (AlS2Pc) and **5-aminolevulinic acid** (ALA) as photosensitizers. AlS2Pc resulted in a panmural photosensitization of the gastric wall, with the highest level encountered in the submucosa. The mucosa and muscularis propria were sensitized to an equal extent. Following light exposure, a full thickness damage resulted. ALA is a natural porphyrin precursor and exogenous administration gave rise to accumulation of protoporphyrin IX (PPIX) in the cells. The resultant pattern of photosensitization was predominantly mucosal and its photodynamic effect was essentially confined to the mucosa. ALA produced a selective photosensitization of the gastric mucosa for its photodynamic ablation with spring the underlying tissue layers.

IT **106-60-5, 5-Aminolevulinic acid**
RL: BIOL (Biological study)
(photosensitization by, of stomach to laser radiation, stomach **tumor** photodynamic **therapy** in relation to)

L24 ANSWER 28 OF 31 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1992:589224 HCAPLUS
DOCUMENT NUMBER: 117:189224
TITLE: Selective accumulation of endogenously produced porphyrins in a liver metastasis model in rats

AUTHOR(S): Van Hillegersberg, Richard; Van den Berg, J. Willem O.; Kort, Will J.; Terpstra, Onno T.; Wilson, J. H. Paul
CORPORATE SOURCE: Med. Fac., Erasmus Univ., Rotterdam, Neth.
SOURCE: Gastroenterology (1992), 103(2), 647-51
CODEN: GASTAB; ISSN: 0016-5085
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The possibility of using the porphyrin precursor **5-aminolevulinic acid** to cause selective porphyrin accumulation in **tumors** was examd. Syngeneic colon carcinomas CC531 were implanted in the livers of Wag/Rij rats. Groups of three to six animals each were given 2 mg/mL of **5-aminolevulinic acid** in drinking water from the 8th, 14th, or 17th day after **tumor** implantation. Two other groups received either 2.5 or 5 mg/kg of Photofrin II (Photomedica Inc., Raritan, NJ) i.v. on day 17. On day 19 the livers were removed and porphyrin concns. were measured in normal livers and **tumors** by solvent extn. and high-performance liq. chromatog. Protoporphyrin accumulated progressively in **tumors** with increasing duration of **5-aminolevulinic acid** administration ($P = 0.0001$), whereas no increase was found in normal livers. After 11 days of **5-aminolevulinic acid** administration the porphyrin concn. ratio between **tumors** and livers was 4:1. In contrast, after Photofrin II administration the concn. was higher in normal livers than in **tumors** (1:3 ratio, **tumor** to liver). Enzyme measurements showed a 3-fold decrease in ferrochelatase activity in **tumors** compared with livers ($P < 0.001$). In conclusion, oral administration of **5-aminolevulinic acid** results in progressive accumulation of protoporphyrin in a transplantable colon carcinoma without accumulation in the surrounding liver tissue. This selective accumulation of porphyrins appears bo be caused by a relative ferrochelatase deficiency in **malignant** tissue. **5-Aminolevulinic acid** administration may be a suitable approach to photosensitizing liver **tumors** for photodynamic **therapy** or for early detection of **tumors** by fluorescence in UV light.

IT **106-60-5, 5-Aminolevulinic acid**
RL: BIOL (Biological study)
(porphyrin accumulation in liver metastasis induced by, photodynamic **therapy** in relation to)

L24 ANSWER 29 OF 31 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1992:566693 HCAPLUS
DOCUMENT NUMBER: 117:166693
TITLE: Endogenous protoporphyrin IX, a clinically useful photosensitizer for photodynamic therapy
AUTHOR(S): Kennedy, James C.; Pottier, Roy H.
CORPORATE SOURCE: Dep. "Oncol.", Queen's Univ., Kingston, ON, K7L 3N6, Can.
SOURCE: J. Photochem. Photobiol., B (1992), 14(4), 275-92
CODEN: JPPBEG; ISSN: 1011-1344
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 96 refs. The tissue photosensitizer protoporphyrin IX (PpIX) is an immediate precursor of heme in the biosynthetic pathway for heme. In certain types of cells and tissues, the rate of synthesis of PpIX is detd. by the rate of synthesis of **5-aminolevulinic acid** (ALA), which in turn is regulated via a feedback control mechanism governed by the concn. of free heme. The presence of exogenous ALA bypasses the feedback control, and thus may induce the intracellular accumulation of photosensitizing concns. of PpIX. However, this occurs only in certain types of cells and tissues. The resulting tissue-specific photosensitization provides a basis for using ALA-induced PpIX for photodynamic **therapy**. The topical application of ALA to certain **malignant** and nonmalignant lesions of the skin can induce a clin. useful degree of lesion-specific

photosensitization. Superficial basal cell carcinomas showed a complete response rate of .apprx.79% following a single exposure to light. Recent preclin. studies in exptl. animals and human volunteers indicate that ALA can induce a localized tissue-specific photosensitization if administered by intradermal injection. A generalized but still quite tissue-specific photosensitization may be induced if ALA is administered by either s.c. or i.p. injection or by mouth. This opens the possibility of using ALA-induced PpIX to **treat tumors** that are too thick or that lie too deep to be accessible to either topical or locally injected ALA.

L24 ANSWER 30 OF 31 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1992:527444 HCAPLUS
DOCUMENT NUMBER: 117:127444
TITLE: Fluorescence distribution and photodynamic effect of **aminolevulinic acid** (ALA)-induced protoporphyrin IX (PP IX) in the DMH rat colonic **tumor** model
AUTHOR(S): Bedwell, J.; MacRobert, A. J.; Phillips, D.; Brown, S. G.
CORPORATE SOURCE: Natl. Med. Laser Cent., Univ. Coll. London, London, WC1E 6JJ, UK
SOURCE: Br. J. Cancer (1992), 65(6), 818-24
CODEN: BJCAAI; ISSN: 0007-0920
DOCUMENT TYPE: Journal
LANGUAGE: English
AB ALA is the 1st committed step in heme synthesis. In the presence of excess ALA, the natural regulatory feedback system is disrupted allowing accumulation of PP IX the last intermediate product before heme and an effective sensitizer. This method of endogenous photosensitization of cells has been exploited for photodynamic therapy (PDT). The fluorescence distribution and biol. effect of induced PP IX were studied in normal and **tumor** tissue in the rat colon. Fluorescence in normal colonic tissue was at a peak at 4 h with a rapid fall off by 6 h. The fluorescence had returned to background levels by 24 h. All normal tissue layers followed the same fluorescence profile but the mucosa showed fluorescent levels 6-fold higher than the submucosa, with muscle barely above background values. At 6 h, the ratio of fluorescence levels between normal mucosa and viable **tumor** was .apprx.1:6. At this time, laser treatment showed necrosis of normal mucosa and **tumor** with sparing of normal muscle. There was good correlation between the fluorescence distribution and the biol. effect of ALA-induced photosensitization on exposure to red light. ALA may be superior to conventional sensitizers for **tumors** that produce heme, as the PP IX is synthesized in **malignant** cells while the other sensitizers mainly localize in the vascular stroma of **tumors**. There is also a greater concn. difference between the PP IX levels in **tumors** and in normal mucosa and normal muscle than with the other photosensitizers, raising the possibility of more selective necrosis in **tumors**.
IT **106-60-5, Aminolevulinic acid**
RL: BIOL (Biological study)
(photodynamic **therapy** with, of colon **tumor** with red laser radiation, protophorphyrin IX induction in relation to)

L24 ANSWER 31 OF 31 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1990:231923 HCAPLUS
DOCUMENT NUMBER: 112:231923
TITLE: Photodynamic and non-photodynamic action of several porphyrins on the activity of some heme-enzymes
AUTHOR(S): Afonso, Susana G.; Chinarro, Sagrario; Munoz, Juan J.; De Salamanca, Rafael E.; Batlle, Alcira M. del C.
CORPORATE SOURCE: Cent. Invest. Porfirinas Porfirias, Univ. Buenos Aires, Buenos Aires, 1056, Argent.
SOURCE: J. Enzyme Inhib. (1990), 3(4), 303-10
CODEN: ENINEG; ISSN: 8755-5093

DOCUMENT TYPE: Journal
LANGUAGE: English
AB The action of porphyrins, uroporphyrin I and III (URO I and URO III), pentacarboxylic porphyrin I (PENTA I), coproporphyrin I and III (COPRO I and COPRO III), protoporphyrin IX (PROTO IX), and mesoporphyrin (MESO), on the activity of **.delta.-aminolevulinic acid** dehydratase, porphobilinogenase, deaminase, and uroporphyrinogen decarboxylase of human erythrocytes in the dark and under UV light was investigated. Both photoinactivation and light-independent inactivation was found in all 4 enzymes using URO I as sensitizer. URO III had a similar action as URO I on porphobilinogenase and deaminase and PROTO IX exerted equal effect as URO I on **.delta.-aminolevulinic acid** dehydratase and uroporphyrinogen decarboxylase. The photodynamic efficiency of the porphyrins was dependent on their mol. structure. Selective photodecompn. of enzymes by URO I, greater specificity of **tumor** uptake by URO I, and enhanced porphyrin synthesis by **tumors** from .delta.-aminolevulic acid, with predominant formation of URO I, underline the possibility of using URO I in detection of **malignant** cells and photodynamic **therapy** .

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L15 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2001 ACS
RN 106-60-5 REGISTRY
CN Pentanoic acid, 5-amino-4-oxo- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Levulinic acid, 5-amino- (8CI)
OTHER NAMES:
CN .delta.-Aminolevulinic acid
CN **5-Aminolevulinic acid**
CN Aminolevulinic acid
FS 3D CONCORD
MF C5 H9 N O3
CI COM
LC STN Files: ADISINSIGHT, AGRICOLA, AIDSLINE, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSNB, DDFU, DIOGENES, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, NAPRALERT, NIOSHTIC, PHAR, PIRA, PROMT, TOXLINE, TOXLIT, USPATFULL

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Other Sources: EINECS**, NDSL**, TSCA**
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29 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
2759 REFERENCES IN FILE CAPLUS (1967 TO DATE)
89 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 134:46702

REFERENCE 2: 134:38926

REFERENCE 3: 134:38347

REFERENCE 4: 134:28247

REFERENCE 5: 134:27009

REFERENCE 6: 134:26992

REFERENCE 7: 134:26991

REFERENCE 8: 134:26474

REFERENCE 9: 134:15050

REFERENCE 10: 134:14439

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L25          20 L23 NOT L24

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L25  ANSWER 1 OF 20  HCAPLUS  COPYRIGHT 2001 ACS
ACCESSION NUMBER:         2000:549696  HCAPLUS
DOCUMENT NUMBER:          134:26992
TITLE:                    In vivo fluorescence kinetics and photodynamic
                          therapy efficacy of .delta.-
                          aminolevulinic acid-induced
                          porphyrins in basal cell carcinomas and actinic
                          keratoses; implications for optimization of
                          photodynamic therapy
AUTHOR(S):                Stefanidou, Maria; Tosca, Androniki; Themelis, George;
                          Vazgiouraki, Eleftheria; Balas, Costas
CORPORATE SOURCE:         Department of Dermatology, Heraklion University
                          General Hospital, Crete, 71110, Greece
SOURCE:                   Eur. J. Dermatol. (2000), 10(5), 351-356
                          CODEN: EJDEE4; ISSN: 1167-1122
PUBLISHER:                John Libbey Eurotext
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
IT   106-60-5, .delta.-Aminolevulinic acid
     RL: BAC (Biological activity or effector, except adverse); BPR (Biological
     process); THU (Therapeutic use); BIOL (Biological study); PROC (Process);
```

USES (Uses)
(fluorescence kinetics and photodynamic **therapy** efficacy of **.delta.-aminolevulinic acid**-induced porphyrins in basal cell carcinomas and actinic keratoses)
REFERENCE COUNT: 19
REFERENCE(S): (1) Abels, C; Br J Cancer 1994, V70, P826 HCAPLUS
(2) Anderson, R; J Invest Dermatol 1981, V77, P13 HCAPLUS
(6) Fijan, S; Br J Dermatol 1995, V133, P282 HCAPLUS
(7) Fritsch, C; Br J Cancer 1999, V79(9/10), P1603 HCAPLUS
(8) Jeffes, E; Arch Dermatol 1997, V133, P727 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 2 OF 20 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:807339 HCAPLUS
DOCUMENT NUMBER: 132:32713
TITLE: Photodynamic destruction of high grade dysplasia and early carcinoma of the esophagus after the oral administration of 5-aminolevulinic acid
AUTHOR(S): Gossner, Liebwin; May, Andrea; Sroka, Ronald; Stolte, Manfred; Hahn, Eckehard G.; Ell, Christian
CORPORATE SOURCE: Department of Medicine II, Klinikum der Landeshauptstadt Wiesbaden, Wiesbaden, 65199, Germany
SOURCE: Cancer (N. Y.) (1999), 86(10), 1921-1928
CODEN: CANCAR; ISSN: 0008-543X
PUBLISHER: John Wiley & Sons, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 46
REFERENCE(S): (5) Ell, C; Gut 1998, V43, P345 HCAPLUS
(11) Gossner, L; Gastroenterology 1998, V114, P448 HCAPLUS
(19) Loh, C; Br J Cancer 1993, V68, P41 HCAPLUS
(30) Peng, Q; Cancer 1997, V79, P2282 HCAPLUS
(37) Sroka, R; J Photochem Photobiol B Biol 1996, V34, P13 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 3 OF 20 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:578139 HCAPLUS
DOCUMENT NUMBER: 132:119322
TITLE: Topical versus systemic **5-aminolevulinic acid** administration for photodynamic **therapy** of the colon in B10.RBP mice
AUTHOR(S): Gil, Maciej; Woszczynski, Marek; Regula, Jaroslaw; MacRobert, Alexander J.; Butruk, Eugeniusz; Bown, Steven G.
CORPORATE SOURCE: Department of Gastroenterology, Medical Center of Postgraduate Education, Warsaw, 02-781, Pol.
SOURCE: J. Biomed. Opt. (1999), 4(3), 286-291
CODEN: JBOPFO; ISSN: 1083-3668
PUBLISHER: SPIE-The International Society for Optical Engineering
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **106-60-5, 5-Aminolevulinic acid**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(topical vs. systemic **5-aminolevulinic acid** for photodynamic **therapy** of colon)
REFERENCE COUNT: 6
REFERENCE(S): (1) Baumgartner, R; First Clinical Experiences in Urology, Proc SPIE 1993, V1881, P20
(2) Bedwell, J; Br J Cancer 1992, V65, P818 HCAPLUS
(3) Chang, S; J Urol (Baltimore) 1996, V155, P1749

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(4) Dougherty, T; Lasers Surg Med 1990, V10, P485 MEDLINE
(6) Regula, J; Gut 1995, V36, P67 MEDLINE
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 4 OF 20 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:449664 HCAPLUS
DOCUMENT NUMBER: 132:90117
TITLE: Effects of photodynamic therapy on human glioma spheroids
AUTHOR(S): Madsen, Steen J.; Sun, Chung-Ho; Chu, Eugene A.; Hirschberg, Henry; Tromberg, Bruce J.
CORPORATE SOURCE: Dep. Health Phys., Univ. of Nevada, Las Vegas, Las Vegas, NV, USA
SOURCE: Proc. SPIE-Int. Soc. Opt. Eng. (1999), 3592(Optical Methods for Tumor Treatment and Detection: Mechanisms and Techniques in Photodynamic Therapy VIII), 52-59
CODEN: PSISDG; ISSN: 0277-786X
PUBLISHER: SPIE-The International Society for Optical Engineering
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **106-60-5, 5-Aminolevulinic acid**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effects of photodynamic **therapy** on human glioma spheroids)
REFERENCE COUNT: 23
REFERENCE(S): (3) Foster, T; Cancer Res 1993, V53, P1249 HCAPLUS
(6) Kaye, A; J Neurosurg 1988, V69, P1 HCAPLUS
(8) Kostron, H; J Photochem Photobiol B: Biology 1996, V36, P157 HCAPLUS
(10) Moan, J; Photochem Photobiol 1991, V53, P549 HCAPLUS
(15) Peng, Q; Cancer 1997, V79, P2282 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 5 OF 20 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:360032 HCAPLUS
DOCUMENT NUMBER: 131:196440
TITLE: Topical and **intratumoral** photodynamic **therapy** with **5-aminolevulinic acid** in a subcutaneous murine mammary adenocarcinoma
AUTHOR(S): Casas, Adriana; Fukuda, Haydee; Meiss, Roberto; Batlle, Alcira M. del C.
CORPORATE SOURCE: Centro de Investigaciones sobre Porfirinas y Porfirias (CIPYP) FCEyN, Ciudad Universitaria, Pabellon II, (University of Buenos Aires) and CONICET, Capital Federal, 1428, Argent.
SOURCE: Cancer Lett. (Shannon, Irel.) (1999), 141(1,2), 29-38
CODEN: CALEDQ; ISSN: 0304-3835
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **106-60-5, 5-Aminolevulinic acid**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(topical and **intratumoral** photodynamic **therapy** with **5-aminolevulinic acid** in mammary adenocarcinoma)
REFERENCE COUNT: 28
REFERENCE(S): (3) Cairnduff, F; Int J Radiat Biol 1995, V67, P93 HCAPLUS
(4) Divaris, D; Am J Pathol 1990, V136, P891 HCAPLUS
(6) Fukuda, H; Cancer J 1992, V5, P295 HCAPLUS
(7) Fukuda, H; Comp Biochem Physiol 1992, V102B, P433

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(9) He, X; Photochem Photobiol 1994, V59, P468 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 6 OF 20 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:349881 HCAPLUS
DOCUMENT NUMBER: 131:141531
TITLE: Rodent fibroblast model for studies of response of malignant cells to exogenous 5-aminolevulinic acid
AUTHOR(S): Li, G.; Szewczuk, M. R.; Raptis, L.; Johnson, J. G.; Weagle, G. E.; Pottier, R. H.; Kennedy, J. C.
CORPORATE SOURCE: Departments of Microbiology and Immunology, Queen's University, Kingston, ON, K7L 3N6, Can.
SOURCE: Br. J. Cancer (1999), 80(5/6), 676-684
CODEN: BJCAAI; ISSN: 0007-0920
PUBLISHER: Churchill Livingstone
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 16
REFERENCE(S): (1) Baserga, R; Ann NY Acad Sci 1992, V660, P64 HCAPLUS
(2) Campbell, D; Photochem Photobiol 1996, V63, P111 HCAPLUS
(3) Campbell, D; Photochem Photobiol 1996, V64, P676 HCAPLUS
(6) Kennedy, J; J Photochem Photobiol B: Biol 1990, V6, P143 HCAPLUS
(7) Kennedy, J; J Photochem Photobiol B: Biol 1992, V14, P275 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 7 OF 20 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:282556 HCAPLUS
DOCUMENT NUMBER: 130:320543
TITLE: Ambulant photodynamic therapy of superficial malignomas with 5-ALA in combination with folic acid and use of noncoherent light
AUTHOR(S): Jindra, Rudolf Hubert; Kubin, A.; Kolbabek, H.; Alth, G.; Dobrowsky, W.
CORPORATE SOURCE: Ludwig Boltzmann Inst. Clinical Oncology Photodynamic Therapy, Vienna, A-1130, Austria
SOURCE: Drugs Exp. Clin. Res. (1999), 25(1), 37-41
CODEN: DECRDP; ISSN: 0378-6501
PUBLISHER: Bioscience Ediprint Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **106-60-5, 5-Aminolevulinic acid**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(photodynamic **therapy** of superficial malignomas with 5-ALA in combination with folic acid and use of noncoherent light)
REFERENCE COUNT: 29
REFERENCE(S): (8) Gomer, C; Cancer Res 1979, V39, P146 HCAPLUS
(9) Hilf, R; Cancer Res 1986, V46, P211 HCAPLUS
(10) Kennedy, J; Photochem Photobiol 1990, V6, P143 HCAPLUS
(11) Kessel, D; Porphyrin Localisation and Treatment of Tumors 1984, P405 HCAPLUS
(12) Klaassen, U; Anti-Cancer Drugs 1998, V9, P203 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 8 OF 20 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:257284 HCAPLUS
DOCUMENT NUMBER: 130:349122
TITLE: Photodynamic **therapy** utilising topical .

delta.-aminolevulinic acid
in non-melanoma skin malignancies of the eyelid and the periocular skin
AUTHOR(S): Wang, Ingrid; Bauer, Birgitta; Andersson-Engels, Stefan; Svanberg, Sune; Svanberg, Katarina
CORPORATE SOURCE: Department of Oncology, Lund University Medical Laser Centre, Lund, Swed.
SOURCE: Acta Ophthalmol. Scand. (1999), 77(2), 182-188
CODEN: AOSCFV; ISSN: 1395-3907
PUBLISHER: Munksgaard International Publishers Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **106-60-5, .delta.-Aminolevulinic acid**
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(photodynamic **therapy** utilizing topical **.delta.-aminolevulinic acid** in non-melanoma skin malignancies of eyelid and periocular skin in humans)
REFERENCE COUNT: 34
REFERENCE(S): (10) El-Sharabasy, M; Br J Cancer 1992, V65, P409 HCAPLUS
(15) Kennedy, J; J Photochem Photobiol B 1990, V6, P143 HCAPLUS
(16) Kennedy, J; J Photochem Photobiol B 1992, V14, P275 HCAPLUS
(17) Kloek, J; Photochem Photobiol 1996, V64, P994 HCAPLUS
(18) Kondo, M; Cell Biol Toxicol 1993, V9, P95 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 9 OF 20 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:136411 HCAPLUS
DOCUMENT NUMBER: 130:206777
TITLE: Cell physiology, biochemistry, and molecular biology of 5-aminolevulinic acid-induced protoporphyrin ix in normal, immortalized, transfected, and malignant cells
AUTHOR(S): Li, Ge
CORPORATE SOURCE: Queen's Univ., Kingston, ON, Can.
SOURCE: (1998) 193 pp. Avail.: UMI, Order No. DANQ27837 From: Diss. Abstr. Int., B 1999, 59(7), 3359
DOCUMENT TYPE: Dissertation
LANGUAGE: English

L25 ANSWER 10 OF 20 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:120479 HCAPLUS
DOCUMENT NUMBER: 130:293341
TITLE: Fluorescence diagnostics and kinetic studies in the head and neck region utilizing low-dose .delta.-aminolevulinic acid sensitization
AUTHOR(S): Wang, Ingrid; Clemente, Laudelina Pais; Pratas, Rui M. G.; Cardoso, Eduardo; Clemente, Manuel Pais; Montan, Sune; Svanberg, Sune; Svanberg, Katarina
CORPORATE SOURCE: Lund University Medical Laser Centre, Lund, Swed.
SOURCE: Cancer Lett. (Shannon, Irel.) (1999), 135(1), 11-19
CODEN: CALEDQ; ISSN: 0304-3835
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 29
REFERENCE(S): (1) Alfano, R; IEEE J Quant Electr 1984, VQE-20, P1507 HCAPLUS
(2) Andersson-Engels, S; IEEE J Quant Electr 1990, V26, P2207 HCAPLUS
(4) Ankerst, J; Appl Spectr 1984, V38, P890 HCAPLUS
(6) Dailey, H; Biochem J 1984, V223, P441 HCAPLUS

(7) Divaris, D; Am J Pathol 1990, V136, P891 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 11 OF 20 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:20701 HCAPLUS
DOCUMENT NUMBER: 130:206770
TITLE: Effect of photodynamic **therapy** using **5-aminolevulinic acid** on 4-nitroquinoline-1-oxide-induced premalignant and malignant lesions of mouse tongue
AUTHOR(S): Ma, G.; Ikeda, H.; Inokuchi, T.; Sano, K.
CORPORATE SOURCE: Second Department of Oral and Maxillofacial Surgery, Nagasaki University School of Dentistry, Nagasaki, 852-8588, Japan
SOURCE: Oral Oncol. (1998), Volume Date 1999, 35(1), 120-124
CODEN: EJCCER; ISSN: 0964-1955
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **106-60-5, 5-Aminolevulinic acid**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effect of photodynamic **therapy** using **5-aminolevulinic acid** on 4-nitroquinoline-1-oxide-induced premalignant and malignant lesions of mouse tongue)
REFERENCE COUNT: 21
REFERENCE(S): (2) Fan, K; Cancer 1996, V78, P1374 HCAPLUS
(6) Henderson, B; Photochemistry and Photobiology 1995, V62, P780 HCAPLUS
(7) Hua, Z; Cancer Research 1995, V55, P1723 HCAPLUS
(8) Jeffes, E; Archives of Dermatology 1997, V133, P727 HCAPLUS
(9) Kennedy, J; Journal of Photochemistry and Photobiology 1990, V6, P143 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 12 OF 20 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:811259 HCAPLUS
DOCUMENT NUMBER: 130:235957
TITLE: In vitro and in vivo porphyrin accumulation by C6 glioma cells after exposure to 5-aminolevulinic acid
AUTHOR(S): Stummer, Walter; Stocker, Susanne; Novotny, Alexander; Heimann, Axel; Sauer, Oliver; Kempski, Oliver; Plesnila, Nikolaus; Wietzorrek, Joachim; Reulen, H. J.
CORPORATE SOURCE: Dep. Neurosurg., Klinikum Grosshadern, Ludwig-Maximilians-Univ., Munich, D-81377, Germany
SOURCE: J. Photochem. Photobiol., B (1998), 45(2-3), 160-169
CODEN: JPPBEG; ISSN: 1011-1344
PUBLISHER: Elsevier Science S.A.
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 40
REFERENCE(S): (1) Anderson, K; Biochim Biophys Acta 1981, V676, P289 HCAPLUS
(3) Bedwell, J; Br J Cancer 1992, V65, P818 HCAPLUS
(6) Divaris, D; Am J Pathol 1990, V136, P891 HCAPLUS
(9) Hanania, J; Cancer Lett 1992, V65, P127 HCAPLUS
(10) Hebeda, K; J Photochem Photobiol B: Biol 1995, V27, P85 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 13 OF 20 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:522666 HCAPLUS
DOCUMENT NUMBER: 129:272382
TITLE: Photodynamic therapy for gastrointestinal tumors using three photosensitizers - ALA induced PPIX, Photofrin

and MTHPC. A pilot study
AUTHOR(S): Mlkvy, P.; Messmann, H.; Regula, J.; Conio, M.; Pauer, M.; Millson, C. E.; MacRobert, A. J.; Bown, S. G.
CORPORATE SOURCE: Department of Gastroenterology, St. Elisabeth Oncological Institute, Bratislava, 812 50, Slovakia
SOURCE: Neoplasma (1998), 45(3), 157-161
CODEN: NEOLA4; ISSN: 0028-2685
PUBLISHER: Slovak Academic Press Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

L25 ANSWER 14 OF 20 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:29719 HCAPLUS
DOCUMENT NUMBER: 128:164434
TITLE: Photodynamic **therapy** with topical .**delta.-aminolevulinic acid** delays UV photocarcinogenesis in hairless mice
AUTHOR(S): Stender, I.-M.; Bech-Thomsen, N.; Poulsen, T.; Wulf, H. C.
CORPORATE SOURCE: Department of Dermatology, University of Copenhagen, Copenhagen, Den.
SOURCE: Photochem. Photobiol. (1997), 66(4), 493-496
CODEN: PHCBAP; ISSN: 0031-8655
PUBLISHER: American Society for Photobiology
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **106-60-5, .delta.-Aminolevulinic acid**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(photodynamic **therapy** with topical **.delta.-aminolevulinic acid** delays UV photocarcinogenesis in hairless mice)

L25 ANSWER 15 OF 20 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1997:723725 HCAPLUS
DOCUMENT NUMBER: 128:99349
TITLE: The kinetics of protoporphyrin fluorescence during ALA-PDT in human **malignant** skin **tumors**
AUTHOR(S): Orenstein, Arie; Kostenich, Genady; Malik, Zvi
CORPORATE SOURCE: Plastic Surgery Department, Sheba Medical Center, Tel Hashomer, 52621, Israel
SOURCE: Cancer Lett. (Shannon, Irel.) (1997), 120(2), 229-234
CODEN: CALEDQ; ISSN: 0304-3835
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **106-60-5, 5-Aminolevulinic acid**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(kinetics of protoporphyrin fluorescence during ALA-PDT in human **malignant** skin **tumors**)

L25 ANSWER 16 OF 20 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1997:691211 HCAPLUS
DOCUMENT NUMBER: 128:31913
TITLE: Effects of fractionated 5-aminolevulinic acid administration on tissue levels of protoporphyrin in vivo
AUTHOR(S): Herman, Mark A.; Webber, John; Luo, Yu; Patacsil, Veronique; Kessel, David; Fromm, David
CORPORATE SOURCE: Department of Surgery, Wayne State University, 6C-University Health Center, 4201 St. Antoine, Detroit, MI, 48201, USA
SOURCE: J. Photochem. Photobiol., B (1997), 40(2), 107-110

CODEN: JPPBEG; ISSN: 1011-1344
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

L25 ANSWER 17 OF 20 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1997:467010 HCAPLUS
DOCUMENT NUMBER: 127:130584
TITLE: In vivo kinetics of ALA-induced fluorescence in the canine oral cavity: influence of drug dose and tissue type
AUTHOR(S): Vaidyanathan, V.; Rastegar, S.; Fossum, T.W.; Flores, P.; Van Der Breggen, E.W.; Egger, N.G.; Jacques, S.L.; Motamedi, M.
CORPORATE SOURCE: Texas AandM University, College Station, TX, 77843, USA
SOURCE: Proc. SPIE-Int. Soc. Opt. Eng. (1997), 2975(Laser-Tissue Interaction VIII), 222-226
CODEN: PSISDG; ISSN: 0277-786X
PUBLISHER: SPIE-The International Society for Optical Engineering
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **106-60-5, 5-Aminolevulinic acid**
RL: ANT (Analyte); BPR (Biological process); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)
(**pharmacokinetics** and safety of **5-aminolevulinic acid** as oral **cancer** photosensitizer)

L25 ANSWER 18 OF 20 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1997:285497 HCAPLUS
DOCUMENT NUMBER: 126:327510
TITLE: Photosensitization of experimental hepatocellular carcinoma with protoporphyrin synthesized from administered .**delta**.-**aminolevulinic acid**: studies with cultured cells and implanted **tumors**
AUTHOR(S): Egger, Norman G.; Schoenecker, James A., Jr.; Gourley, William K.; Motamedi, Massoud; Anderson, Karl E.; Weinman, Steven A.
CORPORATE SOURCE: Department of Preventive Medicine and Community Health, The University of Texas Medical Branch, Galveston, TX, 77555-1109, USA
SOURCE: J. Hepatol. (1997), 26(4), 913-920
CODEN: JOHEEC; ISSN: 0168-8278
PUBLISHER: Munksgaard
DOCUMENT TYPE: Journal
LANGUAGE: English

L25 ANSWER 19 OF 20 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1997:199769 HCAPLUS
DOCUMENT NUMBER: 126:248368
TITLE: Time-dependent intracellular accumulation of .delta.-aminolevulinic acid, induction of porphyrin synthesis and subsequent phototoxicity
AUTHOR(S): Gibson, Scott L.; Havens, James J.; Foster, Thomas H.; Hilf, Russell
CORPORATE SOURCE: Department of Biochemistry and Biophysics, University of Rochester School of Medicine and Dentistry, University of Rochester, Rochester, NY, 14642, USA
SOURCE: Photochem. Photobiol. (1997), 65(3), 416-421
CODEN: PHCBAP; ISSN: 0031-8655
PUBLISHER: American Society for Photobiology
DOCUMENT TYPE: Journal
LANGUAGE: English

L25 ANSWER 20 OF 20 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1995:687111 HCAPLUS
DOCUMENT NUMBER: 123:78663
TITLE: **Photochemotherapeutic** method using **5-aminolevulinic acid** and precursors thereof
INVENTOR(S): Kennedy, James C.; Pottier, Roy H.; Reid, Robert L.
PATENT ASSIGNEE(S): Queen's University, Can.
SOURCE: U.S., 11 pp. Continuation-in-part of U.S. 5, 234, 940.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5422093	A	19950606	US 1993-82113	19930628
US 5079262	A	19920107	US 1989-386414	19890728
US 5211938	A	19930518	US 1991-783750	19911028
US 5211938	B1	19970708		
US 5234940	A	19930810	US 1992-865151	19920408
CA 2126761	AA	19941229	CA 1994-2126761	19940627
US 5955490	A	19990921	US 1995-465242	19950605
PRIORITY APPLN. INFO.:			US 1989-386414	19890728
			US 1991-783750	19911028
			US 1992-865151	19920408
			US 1992-865156	19920408
			US 1993-82113	19930628
			US 1993-92925	19930719

IT **106-60-5, 5-Aminolevulinic acid**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**photochemotherapeutic** methods using **5-aminolevulinic acid** and precursors)

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FILE LAST UPDATED: 11 Jan 2001  (20010111/ED)

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Now you can extend your author, patent assignee, patent information,
and title searches back to 1907.  The records from 1907-1966 now have
this searchable data in CAOLD.  You now have electronic access to all
of CA: 1907 to 1966 in CAOLD and 1967 to the present in HCAPLUS on STN.


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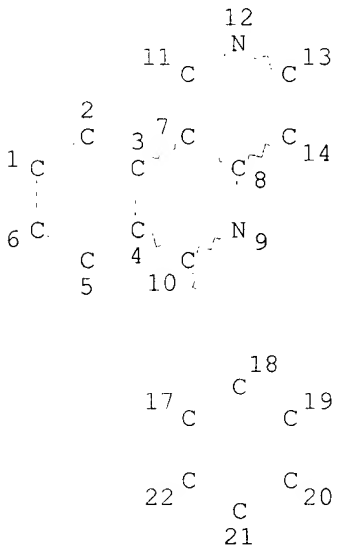


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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
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NUMBER OF NODES IS  20

STEREO ATTRIBUTES: NONE
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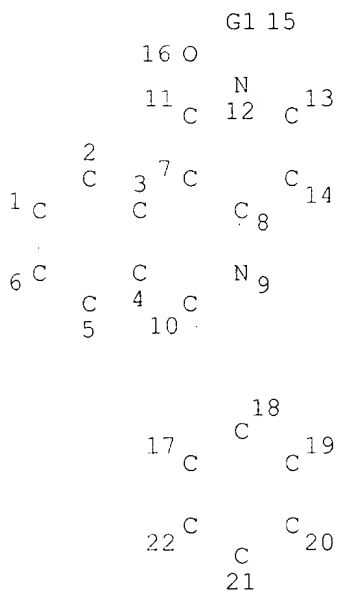
L6 STR



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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
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STEREO ATTRIBUTES: NONE
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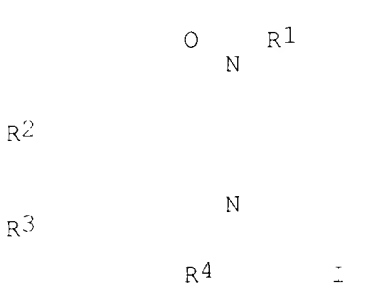
=> d ibib abs hitrn l8 1-2

L8 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:161279 HCAPLUS
DOCUMENT NUMBER: 132:194380
TITLE: Preparation of tetrazolylphenylbenzonaphthyridine N-oxides having phosphodiesterase-3 and phosphodesterase-4 inhibiting activity.
INVENTOR(S): Gutterer, Beate; Amschler, Hermann; Ulrich, Wolf-rudiger; Martin, Thomas; Bar, Thomas; Hatzelmann, Armin; Boss, Hildegard; Beume, Rolf; Bundschuh, Daniela; Kley, Hans-peter; Flockerzi, Dieter
PATENT ASSIGNEE(S): Byk Gulden Lomberg Chemische Fabrik Gmbh, Germany
SOURCE: PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2000012501 A1 20000309 WO 1999-EP6139 19990821
W: AE, AL, AU, BA, BG, BR, CA, CN, CZ, EE, GE, HR, HU, ID, IL, IN, JP, KR, LT, LV, MK, MX, NO, NZ, PL, RO, SG, SI, SK, TR, UA, US, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
AU 9959701 A1 20000321 AU 1999-59701 19990821
PRIORITY APPLN. INFO.: EP 1998-116416 19980831
WO 1999-EP6139 19990821
OTHER SOURCE(S): MARPAT 132:194380
GI



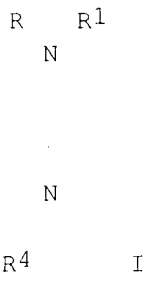
AB Title compds. [I; R1 = alkyl; R2, R3 = OH, alkoxy, cycloalkoxy, cycloalkylmethoxy, fluoroalkoxy; R2R3 = alkylenedioxy; R4 = (substituted) tetrazolylphenyl], were prepd. Thus, (-)-cis-3-(3-ethoxy-4-methoxyphenyl)-4-[4-(2H-2-tetrazol-5-yl)benzamido]-1-methylpiperidine (prepn. given) was refluxed 16 h with POCl3 in MeCN to give (-)-cis-9-ethoxy-8-methoxy-2-methyl-6-[4-(2H-2-ethyltetrazol-5-yl)phenyl]-1,2,3,4,4a,10b-hexahydrobenzo[c][1,6]-naphthyridine. This was stirred with H2O2 in MeOH to give cis-9-ethoxy-8-methoxy-2-methyl-6-[4-(2H-2-ethyltetrazol-5-yl)phenyl]-1,2,3,4,4a,10b-hexahydrobenzo[c][1,6]-naphthyridine 2-N-oxide. The latter inhibited PDE4 and PDE3 with -log IC50 = 7.53 and 6.11, resp.
IT **259742-22-8P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of tetrazolylphenylbenzonaphthyridine N-oxides having phosphodiesterase-3 and phosphodesterase-4 inhibiting activity)
REFERENCE COUNT: 2
REFERENCE(S): (1) B Gulden Lomberg Chem Fab; WO 9821208 A 1998 HCAPLUS
(2) Byk Gulden Lomberg Chem Fab; WO 9821208 A 1998 HCAPLUS

L8 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:723035 HCAPLUS
DOCUMENT NUMBER: 131:322611
TITLE: Preparation of N-oxidohexahydrobenzo[c][1,6]naphthyridines as PDE3 and PDE4 inhibitors
INVENTOR(S): Gutterer, Beate; Amschler, Hermann; Ulrich, Wolf-Rudiger; Martin, Thomas; Bar, Thomas; Hatzelmann, Armin; Boss, Hildegard; Beume, Rolf; Bundschuh, Daniela; Kley, Hans-Peter; Flockerzi, Dieter
PATENT ASSIGNEE(S): Byk Gulden Lomberg Chemische Fabrik G.m.b.H., Germany
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE

WO 9957118	A1	19991111	WO 1999-EP2827	19990427
W: AE, AL, AU, BA, BG, BR, CA, CN, CZ, EE, GE, HR, HU, ID, IL, IN, JP, KR, LT, LV, MK, MX, NO, NZ, PL, RO, SG, SI, SK, TR, UA, US, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9939289	A1	19991123	AU 1999-39289	19990427
PRIORITY APPLN. INFO.:			EP 1998-108124	19980505
			WO 1999-EP2827	19990427

OTHER SOURCE(S): MARPAT 131:322611
GI



I

AB Title compds. [I; R = oxido; R1 = alkyl; R2,R3 = H, (fluoro)alkoxy, cycloalkyl(meth)oxy; R2R3 = alkylenedioxy; R4 = C6H3R5R6; R5 = H, halo, alkyl, alkoxy, etc.; R6 = CO2H, alkoxycarbonyl, (di)(alkyl)amino, etc.] were prepd. Thus, (-)-cis-4-amino-3-(3-ethoxy-4-methoxyphenyl)-1-methylpiperidine was amidated by 4-[(Me2HC)2N]C6H4COCl and the product cyclized to give cis-I [R1 = Me, R2 = OEt, R3 = OMe, R4 = C6H4[N(CHMe2)2]-4](II; R = null) which was treated with H2O2 to give II (R = oxido). Data for biol. activity of I were given.

IT **249287-38-5P 249287-39-6P 249287-40-9P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of N-oxidohexahydrobenzo[c][1,6]naphthyridines as PDE3 and PDE4 inhibitors)

REFERENCE COUNT: 1
REFERENCE(S): (1) Sandoz; EP 0247971 A 1987 HCAPLUS

=>

=>

=> fil caold

FILE 'CAOLD' ENTERED AT 16:56:10 ON 12 JAN 2001
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FILE COVERS 1907-1966
FILE LAST UPDATED: 01 May 1997 (19970501/UP)

This file contains CAS Registry Numbers for easy and accurate substance identification. Title keywords, authors, patent assignees, and patent information, e.g., patent numbers, are now searchable from 1907-1966. TIFF images of CA abstracts printed between 1907-1966 are available in the PAGE display formats.

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L9 0 L7

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STRUCTURE FILE UPDATES: 11 JAN 2001 HIGHEST RN 313639-92-8
DICTIONARY FILE UPDATES: 11 JAN 2001 HIGHEST RN 313639-92-8

TSCA INFORMATION NOW CURRENT THROUGH July 8, 2000

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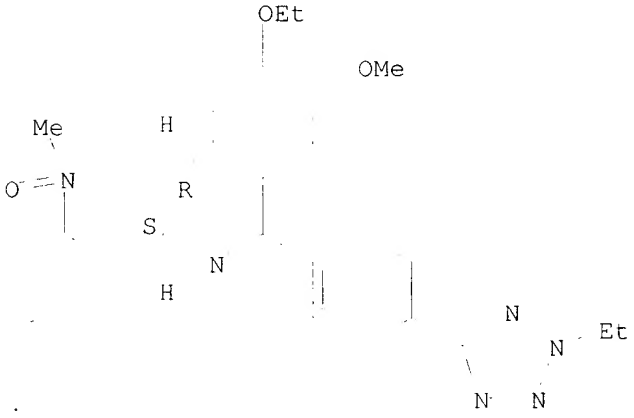
=> d ide can l7 1-2

L7 ANSWER 1 OF 4 REGISTRY COPYRIGHT 2001 ACS
RN 259742-22-8 REGISTRY
CN Benzo[c][1,6]naphthyridine, 9-ethoxy-6-[4-(2-ethyl-2H-tetrazol-5-yl)phenyl]-1,2,3,4,4a,10b-hexahydro-8-methoxy-2-methyl-, 2-oxide, (4aR,10bS)-rel- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C25 H30 N6 O3
SR CA
LC STN Files: CA, CAPLUS

Relative stereochemistry.



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:194380

L7 ANSWER 2 OF 4 REGISTRY COPYRIGHT 2001 ACS
RN 249287-40-9 REGISTRY
CN Benzamide, N,N-dibutyl-4-[(4aR,10bS)-1,2,3,4,4a,10b-hexahydro-8-methoxy-2-methyl-2-oxido-9-propoxybenzo[c][1,6]naphthyridin-6-yl]-, rel- (9CI) (CA INDEX NAME)
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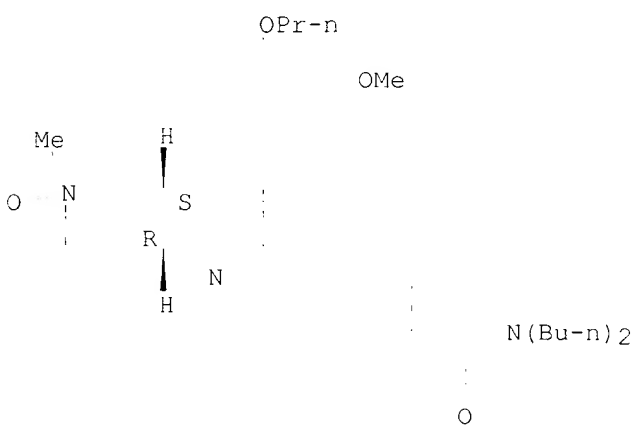
MF C32 H45 N3 O4
SR CA
LC STN Files: CA, CAPLUS

Relative stereochemistry.



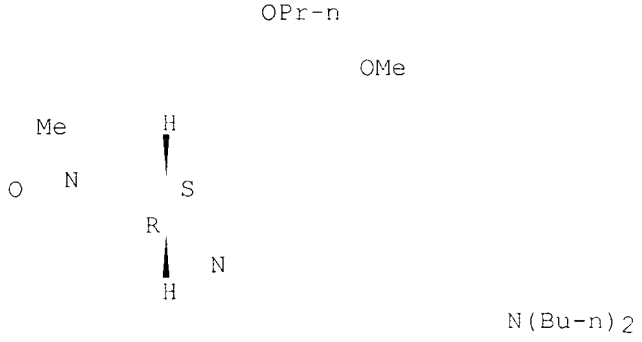
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 131:322611

=> d ide can l7 2-4

L7 ANSWER 2 OF 4 REGISTRY COPYRIGHT 2001 ACS
RN 249287-40-9 REGISTRY
CN Benzamide, N,N-dibutyl-4-[(4aR,10bS)-1,2,3,4,4a,10b-hexahydro-8-methoxy-2-methyl-2-oxido-9-propoxybenzo[c][1,6]naphthyridin-6-yl]-, rel- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C32 H45 N3 O4
SR CA
LC STN Files: CA, CAPLUS

Relative stereochemistry.

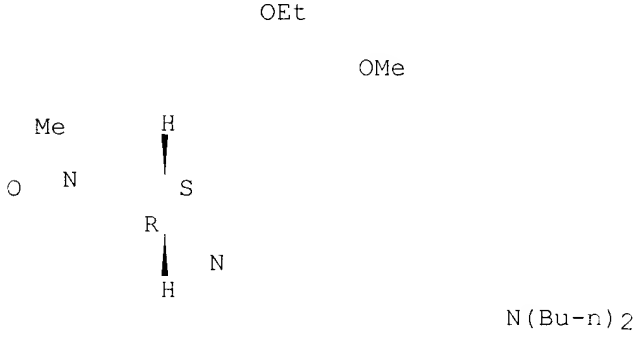


1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 131:322611

L7 ANSWER 3 OF 4 REGISTRY COPYRIGHT 2001 ACS
RN 249287-39-6 REGISTRY
CN Benzamide, N,N-dibutyl-4-[(4aR,10bS)-9-ethoxy-1,2,3,4,4a,10b-hexahydro-8-methoxy-2-methyl-2-oxidobenzo[c][1,6]naphthyridin-6-yl]-, rel- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C31 H43 N3 O4
SR CA
LC STN Files: CA, CAPLUS

Relative stereochemistry.

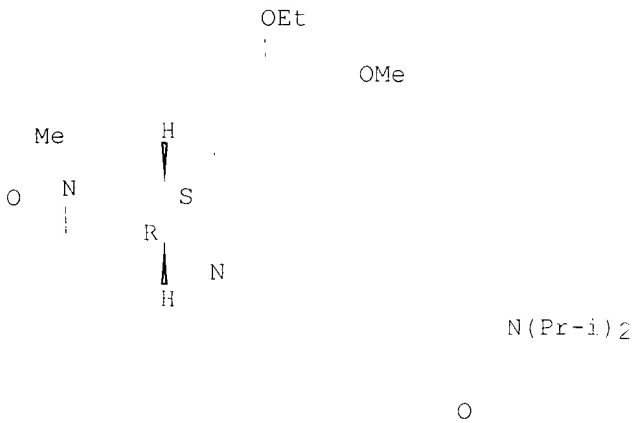


1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 131:322611

L7 ANSWER 4 OF 4 REGISTRY COPYRIGHT 2001 ACS
RN 249287-38-5 REGISTRY
CN Benzamide, 4-[(4aR,10bS)-9-ethoxy-1,2,3,4,4a,10b-hexahydro-8-methoxy-2-methyl-2-oxidobenzo[c][1,6]naphthyridin-6-yl]-N,N-bis(1-methylethyl)-, rel- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C29 H39 N3 O4
SR CA
LC STN Files: CA, CAPLUS

Relative stereochemistry.



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 131:322611